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EDITORIAL

Have you ever looked forward at the commencement of a school year and visioned all the knowledge you will garner in the five thousand odd hours spent in the outer strata of an academic atmosphere?

Have you ever looked back upon those same hours and considered them minutes; and upon that knowledge and summarized it in one thought?

Only as we come to graduation do we realize that—

"All experience is an arch wherethro'
gleams that untravelled world,
Whose margin fades forever and forever when I move."

All the hopes of vast intellectual accomplishments which we visioned as ours in the college years to come, have not been realized — and so we leave, down-hearted, but wiser men. Undergraduate days are valuable, not for the knowledge gained, but for the systems constructed and the wisdom earned,

whereby we realize our true rank among the wise.

But we must not feel badly about it. Rather resume, with a richer enthusiasm than that we had on first entering the Halls of Learning and welcome the vast sea of experience which lies before. The desire to specialize is pathognomic of intellectual senility.

To those of you who are reading these columns for the last time as undergraduates, may success in the future be yours. The most dismal failure in the practice of medicine is the man who is so busy as to have time only for a penny-in-the-slot practice. Each patient in one's early years of practice offers more to the student-physician than the entire six years of undergraduate work. Don't worry about the future—be sincerely interested in the present.

A doctor's only investment should be his brain and his health. Organized leisure, not too much, but enough, spent regularly in an exhilarating atmosphere will do much to fire you with the enthusiastic energy by which you will be able to accomplish much and well. Time for reading, not only of medical science but about mankind is worth more than any stock offered to the speculator of to-day—or of to-morrow.

When you find that your plans, determined upon in good faith, are becoming blurred, call a halt—marshal your forces—and don't forget that perhaps an assistant is the answer to your problem.

This issue of the Journal marks the end of Volume 13. We hope that this volume has not fallen short of the high standard set in previous years. Several minor innovations have been made this year, including the publication of abstracts of current literature and a division of Editorial responsibility. We feel that the latter change has been an important one. Each member of the editorial staff has been responsible for one issue of the Journal. This has not only lessened the labours of the Editor-in-Chief, but has also given the other editors a more practical interest in the Journal. We would like to take this opportunity of thanking every member of the editorial staff for their unfailing assistance. Thanks are also due to the Managing Editor, Mr. Hugh Bright, to his assistant, Mr. Sturgeon, and to all the year representatives for their help in distributing the Journal.

Next year the Journal will enter upon a new era of progress. It is hoped that the recent changes in the Constitution will make possible improvement in the size and quality of the magazine. During this important period of expansion, the Journal will be under the able guidance of Mr. Hugh Hayward, assisted by Mr W. G. Bigelow. We retire with every confidence that next year will be one of the most successful in the history of the Journal.

For ten years, Mr. Avila Paré, of the Extension Print, has looked after the printing of the Journal. He has taken a personal interest in the Journal and given service such as mere money cannot purchase. Certainly no one person has had more to do with the continued success of the Journal than has Mr. Paré. We most heartily thank him for his past efforts and hope that he will long continue to help us with the Journal.

CHRONIC ARTHRITIS

By A. A. FLETCHER, M.B., F.R.C.P. (C.)

Chronic arthritis, in its broadest sense, is used to cover a large number of joint disorders, varying both in their aetiology and clinical picture. There is, however, a tendency to-day to confine the term to the two great types of joint reaction of unknown aetiology, rheumatoid arthritis and osteo-arthritis.

It seems likely that these chronic joint affections constitute the greatest cause of disability throughout the middle and cold temperature zones. Recent house-to-house surveys have revealed that in many localities between 3 per cent. and 4 per cent. of the population suffer from rheumatism and joint affections. This figure exceeds that of tuberculosis, heart disease and cancer combined. Our interest now awakened, chronic arthritis bids fair to be the Cinderella of modern medicine.

Because the aetiology of these diseases is subject to continual controversy, there has been as yet no general agreement either as to classification or nomenclature. But the broad division of chronic arthritis into those of known aetiology and those of unknown aetiology, and the further subdivision of the latter class into two general groups forms the basis of most classifications to-day. The following grouping is based on this principle:

Chronic Arthritis of Known Aetiology.

1. Infectious.
   - Tuberculous.
   - Gonococcal.
   - Syphilitic.
   - Influenzal.
   - Staphlococcal.
   - Streptococcal, and many others.

   (Most of these will present a periarticular joint reaction, suppurative or non-suppurative).
2. Traumatic.
3. Neuropathic.
   - Charcot's joint.
4. Metabolic.
   - Gout.
   - Haemophilia.

Chronic Arthritis of Unknown Aetiology.

1. Rheumatoid arthritis (variously called: atrophic, non-specific, infectious, periarticular, proliferative).
2. Osteo-arthritis (also called: hypertrophic arthritis, degenerative arthritis, senile arthritis).
3. Sometimes a separate group is added comprising the arthritis which occurs almost solely in women, most often developing about the time of the catamenia, and characterised from the start by proliferation of the synovial membrane; *Menopausal or Villous Arthritis.*

Chronic arthritis of the spine may also be divided into the two groups:

1. Rheumatoid or ankylosing spondylitis (Marie Strumpell, after the two original descriptions of the disease).
2. Osteo-arthritic spondylitis.

Rheumatoid Arthritis.

Clinical picture. This disease in its classical form presents a multiple joint involvement, most often appearing in the proximal phalangeal joints where the fusiform or spindle-like periarticular swelling is rarely simulated by any other condition. However, wide clinical variations are met with. For example: one or two joints only may be involved, the shoulder, hip or knee; or there may be little or no swelling; or in other cases invasion of fibrous tissue in and about the joint may be the most prominent feature. But always this type of disease will, in its early stage, present a soft tissue or periarticular

reaction, while cartilage and bone changes will appear only at a later stage. Along with this periarticular change most cases will show a varying degree of muscle atrophy and muscle spasm, weakening and limiting the movement of the joint. On these two signs, spasm and atrophy, dependence at times must be placed for the diagnosis of lesions of deep-seated joints, such as the hip or spine.

The mode of onset is most variable; sometimes the disease begins insidiously, and many months or even years may elapse before the condition is fully developed; on the other hand, the disease may begin with an acute and general polyarthritis. At times a flitting arthritis may be the initial feature, which may suggest rheumatic fever, but before long the disease settles down, loses its migratory character, and goes on to permanent structural joint damage.

Pain and stiffness are usually complained of. As a rule these symptoms are worse in the morning or after immobilization, and the patient may be highly susceptible to climatic changes, with aggravation of the joint symptoms in cold and damp weather. Fever may be present in the more acute cases or during a relapse, but at other times is notably absent. As the disease progresses to the later stages, fibrosis and ankylosis make their appearance. Rarely, the disease may go on to end stage deformity and total invalidism.

The X-ray findings during the early stage may be that of a normal joint picture. Sometimes the periarticular swelling may be made out, if it is marked. But, at a later stage when bone atrophy sets in, rarefaction of bone becomes apparent in the decreased depth of the articular bone shadows. At the same time, destructive changes in the cartilage may be recognized in the thining or disappearance of joint spacing and destructive changes on the articular surfaces or, occasionally, cyst-like areas of rarefying osteitis may be made out, varying from minute punched-out spots to those the size of a pea or bean.

Aetiology. No general survey of the incidence of the disease has as yet been carried out. Plans are at present on foot for collecting data in many countries, including Canada. There is no doubt that toward the tropics the disease does not develop to any extent, whereas it meets its highest incidence in cold and damp regions. The onset is usually in the late winter. The disease may occur at any age, but commences most usually between twenty and forty, and its incidence in women as compared to men is somewhere between three and five as to one. In children, it occurs about equally in both sexes and may take on a grave form, Still's disease. We are still at a loss to account for the exact nature of the joint processes. The usual theories are those of: (1) bacterial infection; (2) toxaemia; (3) allergy; and perhaps (4) a virus or unknown agent. Recent bacteriological studies have gone far in supporting the impression created by the clinical picture that the disease is one of infection. For example, the serum of over 75 per cent. of cases agglutinates haemolytic streptococci at a high titre, whereas control sera rarely show agglutinins at any significant level. But this and other allied observations demonstrate only that the rheumatoid arthritic patient is subject to haemolytic streptococcal infection. It does not prove that the organism is the cause of the arthritis. At other times, other infective illnesses appear to initiate or aggravate the disease, and we feel by no means sure that other organisms may not play a rôle similar to that of the haemolytic streptococcus. In this connection, mention must be made of the hypothesis of focal infection. The rheumatoid arthritic patient appears liable to develop and harbour foci of infection and, undoubtedly, the persistence of this focal infection appears to prolong convalescence while the radical removal — *on occasion* — is followed by striking improvement.

Such experience, however, does not justify the significance with which focal infection is sometimes invested, nor has it been possible to attribute to these foci a basic or casual rôle in the development of the disease. Recent evidence would rather persuade us that an intact mucous membrane may be the site of bacterial localization of as much significance as closed foci. Further than this, foci which appear to precipitate a recrudescence of joint disease may furnish on culture different bacteria: haemolytic streptococci, streptococcus viridans, staphlococci, B. coli, etc. Many individuals, both in health and with other diseases, harbour foci of infection and we must assume the influence of other casual factors. Among these we may recognize heredity, constitution, unsuitable occupation, chronic fatigue, malnutrition, psychoneurotic upset, metabolic and endocrine disorder, other illnesses, repeated pregnancies, gastrointestinal disturbances, and almost any form of persistent ill-health or debility.

Pathology. Our knowledge of the pathology of rheumatoid arthritis is largely based on studies of cases which have come to autopsy at an end or quiescent stage, and no clear insight into the sequence of events that takes place is brought out by these observations. From the standpoint of the clinic, rheumatoid arthritis is a disease of stages and much of our treatment is influenced by the character of the joint reaction as the disease advances.

In the initial stage, the periarticular tissues are oedematous and characteristic focal collections of lymphocytes are seen in the synovial membrance. In the intermediate stages, proliferation is the dominant reaction. Fibrous tissue increases in and about the joints. The synovial membrane undergoes thickening. The cartilage tissue is invaded by and replaced by granulation tissue, referred to as pannus. In the later stage of the disease all evidence of inflammation may be lacking and the changes largely result from the scarring and deforming influence of fibrous tissue.

Treatment. In the treatment of rheumatoid arthritis, emphasis should be placed upon the chronic character of the illness and its multiple aetiology. The outcome will largely depend upon our ability to search out and combat the various exciting and predisposing factors which influence the development of the disease. During the early stage, the patient should be at rest. This is a period when symptoms may be mild. The importance of rest may not be fully realized and adequate protection of the patient may be postponed until the joints have undergone permanent pathological damage. At the early stage, six to ten weeks in bed is often sufficient for subsidence of the disease, and our greatest need to-day is hospital facilities to care for these patients when recovery may be confidently anticipated. When the acute stage is passed, rest is not so important, but the principles of protection from physical and nervous fatigue, unfavourable environment, occupation, etc., are still requisite. At this stage, massage, physiotherapy, and hydrotherapy are helpful in raising the resistance of the patient to infection and in improving general health. At a late stage, activity is much more indicated than rigid rest. This often taxes our ingenuity in view of the chronic invalidism, joint deformity and ankylosis which may be present at this stage. Often much assistance may be obtained from the occupational therapist.

The question of focal infection constitutes a problem in judgment as it does perhaps in no other disease. At the early stage a complete survey should be carried out. Teeth, tonsils, sinuses, gall-bladder, colon, genito-urinary tract, particularly the prostate, all call for careful review. When a focus is undoubtedly the site of a suppurative process, treatment—radical if possible—is indicated; but there is to-day a swing toward conservatism on the part of the profession in their at-

titude toward suspicious foci and the feeling is more general now that teeth or tonsils, for example, should not, by and large, be removed on the basis of some ill-grounded doubt. At times, persistent mucous membrane infection may be an expression and not a cause of the patient's ill-health.

There can be no question that climate and the patient's reaction to his environment will have a profound influence on his progress and many patients find it profitable to spend some weeks in the South or, in the more obstinate cases, to spend the entire winter in a more benign climate than our own. If, for various reasons, the patient remains in the North, some protection from the cold and damp may be afforded by the wearing of warm clothing, the use of radiant and other thermal measures. Later, some attempt should be made to decrease the patient's susceptibility to cold. Massage, hydrotherapy such as mild contrast baths, sunlight and out-door life, along with improved general health, will add to the patient's power of adaptation to a climate such as ours.

In a chronic infective disease associated often with varying degrees of undernutrition, the prescription of a suitable dietary regimen demands careful consideration. In general, a patient's diet should be abundant in protective food factors, adequate in protein of good biological value, rich in vitamin,—fresh fruit, fresh vegetables, and dairy products. God liver oil or haliver oil may be added; yeast; and, at times, wheat germ. Calories may be allowed freely, given as cream and butter. Many patients do well when carbohydrate is restricted and, in those who are overweight, some general restriction in calories is beneficial. But the problem of nutrition may be much more complex. Gastro-intestinal dysfunction may be a prominent feature of the patient's illness. Various forms of food idiosyncrasy, dyspepsia, bowel atony and colon instability are commonly met with. Sometimes improvement in colon motility may be brought about by the use of vitamin B in the form of yeast, and many patients with unstable colons do best on smooth, non-irritating diets.

Closely allied to the problem of nutrition is that of bowel hygiene. The use of laxatives and enemas is likely to be overdone and may do more harm than good. When possible, improved digestion and colonic function are best brought about by diet and the simpler measures.

At times, endocrine therapy may be called for, and many patients with low metabolic rates appear to be helped by thyroid extract. This is most frequently the case in those whose arthritis of any type develops about the period of the menopause. We have, as yet, no other endocrine preparation of any proven value in the treatment of this disease. Drugs, such as acetylsalicylic acid and codeine, are by long odds the most dependable measures for the relief of pain. Other drug stuffs have their supporters — arsenic, sulphur and gold—but their value is uncertain. The anaemia of arthritis is rarely a true iron deficiency anaemia, but iron may be worthy of a trial when anaemia is present.

Vaccines are still widely used in the treatment of rheumatoid arthritis but it is most important that this form of therapy should be looked on as an adjuvant to treatment. Formerly vaccine treatment was subject to much abuse and patients were often more harmed than helped. Much the greatest improvement in vaccine treatment to-day is the change toward the small dose used over a longer period of time. The dose given should not be large enough to cause a systemic reaction, and might be reduced to use one-hundredth of a usual vaccine injection. As a rule, stock vaccines are made with some strain of streptococcus. No special advantage has been demonstrated for the use of autogenous vaccines. Given cautiously, vaccine therapy seems to favorably modify the course of arthritis

at times, but as a rule good results may be obtained without their use.

Local Measures in Treatment. So far no reference has been made to the treatment of the joints themselves. Here we are concerned with (1) the relief of pain, and (2) with the prevention of damage, deformity, and ankylosis. During the acute stage splinting may be applied, at first for the whole day, and then for part of the day, for the relief of pain, but it is better to keep the patient in bed without splints. In the intermediate stage, movement is gradually started. The flow of synovial fluid is increased; the nutrition of the body improved; cicatricial and degenerative damage to the joint reduced if the joint is passively moved throughout its range of movement. The adjustment between immobilization and movement calls for nice judgment, and the joints should be more actively used as the inflammatory process subsides. Weight bearing is allowed last. Movement without weight bearing is a good prescription. During the intermediate stage, heat, diathermy and light may all add to the patient's comfort. Special forms of manipulation may be called for, but this is too complicated a field to be dealt with here. The correction of deformity is a field for the orthopaedist.

Osteo-Arthritis.

Clinical Picture. Osteo-arthritis is a joint disease of middle and later life. Rarely seen before forty years of age, it is widely prevalent among elderly people who demand much of their joints.

Typically, the onset is gradual, and following some repeated strain or injury the joint becomes painful and perhaps stiff. The earliest pathological change appears to be in the cartilage, which undergoes fibrillation or erosion. But the more prominent clinical feature is the formation of new bone, which appears as osteophytic growths or lipping at the margins of the articular surfaces. The primary degenerative cartilage change and secondary hypertrophic bone change may long precede the appearance of pain, which may be associated with a late stage thickening of the periarticular tissues.

As compared with rheumatoid arthritie, fewer joints are involved. The disease not uncommonly is confined to one or two joints such as the knee or hip.

These patients are often well developed, over-weight, and present little evidence of systemic disease. This is in striking contrast to rheumatoid arthritis, which might well be viewed as a general illness with joint manifestations.

Osteo-arthritis will present from the start a characteristic X-ray picture,—thinning of the joint space, marginal lipping, or spur formation, and areas of condensing or rarefying osteitis in and about the joint surfaces.

Aetiology. Many factors appear to contribute to this type of joint reaction. While some physical factor seems to determine its onset, behind this premature degenerative joint change there must be influences which as yet are not clearly understood. Possibly the basic state is similar to that which underlies arteriosclerosis. Many of our patients are unduly aged and show capillary and small vessel disease, and hypertension.

The menopause will sometimes precipitate the arthritis, and at other times the patient may be definitely hypothyroid. Undernutrition will seldom seem to be a cause.

There is still much doubt as to whether there is a toxic or infective factor. There are those who see in the disease an early reaction to wear and tear, or in other words, a primary degenerative process, and others who see in the disease a secondary degenerative reaction to some toxic, infective, or metabolic injury to the joint. At any rate, clinically, any chronic, infective, or toxic factor will certainly accelerate and probably predispose to this type of joint disease.

Pathology. There is not much to add regarding pathology. The initial cartilage change, fibrillation, or destruction, and the bone overgrowth (marginal lipping), have been described. Condensation of bone also occurs where it is stripped of its cartilage and may present an ivory-like hardness (eburnaton).

Treatment: The treatment of osteoarthritis calls for measures which (1) will protect the joints from further damage and (2) those which will improve the circulation in the joint, and (3) which will clear up any infective toxic, or metabolic influence.

General measures of treatment, such as those used in rheumatoid arthritis, are not indicated. It is the joint that requires rest, not the patient, and even minimal repeated traumata must be avoided.

Local physical measures such as radiant heat, diathermy, and later, massage and various forms of hydrotherapy may be helpful and as the disease subsides, passive and active movements, but weight bearing is best avoided or restricted.

In patients who are overweight, reduring diets are of value both in their weight sparing influence upon these joints and as a result of beneficial action of weight reduction in degenerative disease. Those with poor bowel motility will do well on diets containing liberal amounts of roughage, yeast, raw vegetables, raw fruits, if such measures do not bring about bowel irritation.

Drugs have little value except for the reief of pain. Thyroid extract is often worthy of a trial.

In spite of a belief that these patients are suffering from a purely degenerative disease, they do best in warm climates and the avoidance of cold and damp will add much to their comfort.

Focal infection should be carefully sought for and treated, but the removal of such foci will not offer much prospect of any striking or immediate relief.

As to vaccines, there seems little justification for their use in osteoarthritis.

In the more advanced cases, especially with involvement of the knees or hips, special orthopaedic and surgical procedures may be necessary.

Finally reference should be made to Heberden's Nodes,—those split-pea-like nodosities at the proximal end of the distal phalangeal joints. These develop most often in women at the time of the menopause and represent an exceedingly benign type of arthritis.

No attempt has been made to discuss differential diagnosis. Gout and gonococcal arthritis are those which are most often confused with the two great types above described. Villous arthritis is often associated with osteoarthritis, but may be a disease, sui generis. It rarely goes on to the invalidism or distress brought about by rheumatoid arthritis.

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SPONDYLOLISTHESIS

By H. V. RICE, '36

Spondylolisthesis is an anterior displacement of one vertebra on the one beneath it. The common site for it to occur is at the lumbosacral joint, and by custom the term is usually applied to displacement in this region. Infrequently other parts of the spinal column are affected.

Historical Note.

It is reported that in 1782, Herbinieau described a condition now believed to have been spondylolisthesis. The first definite record and description of it, however, was given by Kilian in 1853. During the latter part of the last century a great deal of work on it was done by Lambl, Herrgott, Hegar and others. It was mainly important then, because of the frequent obstruction to labour that it caused, and most of the early cases were reported in women. The present occurrence of the condition is equal in the two sexes. As is the case with a great many conditions, the incidence of it is greater than was at first considered. Whereas Halbee estimated from the literature in 1923 that up to that time there had been reported about 200 cases in all, there is no doubt that at the present time this figure greatly under-estimates the frequency with which it is met.

Pathology.

An advanced case presents a typical picture. The body of the fifth lumbar vertebra lies anterior to the plane that it normally occupies. This is shown by the fact that the curve formed by the anterior surface of the vertebral bodies is broken at the point of dislocation, the anterior surface of the fifth lumbar overhanging the body of the sacrum. This dislocation might be only slight, or it may be great, so that the fifth lumbar comes to lie anterior to the upper sacral segments, when the condition is referred to as a spondyloptosis. In the intermediate stages, the fifth lumbar body is tilted forward upon the upper surface of the sacrum, in the manner that the French describe as the "chapeau de gendarme renversee." The whole vertebral column is displaced with the affected vertebra, so that the body becomes shorter, there is a lumbar lordosis, and the crests of the ilia are close to the lower ribs, and on lateral flexion, the latter pass within the false pelvis. In the affected vertebra, the superior articular facet and the root of the arch, and the transverse process are carried forward with the body. But the inferior articular facet and the laminae and dorsal spine remain in their normal relationship to the sacrum. This is made possible by a separation of the arch at the pedicle, between the superior and inferior articular facets. The separation may become so great that the fourth lumbar body comes to be pressed through the space and lies on the upper surface of the sacrum. Where abnormal body surfaces come in contact, there may be bony proliferation. The most common site for this to occur is on the anterior lip of the sacrum, where a shelf forms in an effort to extend the promontory and increase the bearing area.

Microscopical pathological findings in the region of the separation at the pedicle are insignificant as a rule. There is seldom callus, usually only fibrous tissue bridging the gap of the separation, and occasionally hemorrhages into this.

The condition is rarely unilateral. Occasionally also the anterior dislocation of the whole fifth lumbar verterbra occurs as a result of a fracture through the superior articular processes of the sacrum and part of these processes are

carried forwards with the lower articular processes of the fifth lumbar vertebra.

The axis of the sacrum is tilted backwards, so that its longitudinal upper surface is more nearly horizontal. With this goes a tilting of the pelvis, so that the iliac crests are almost horizontal, and the anterior superior spines approach the level of the posterior superior spines.

Symptomatology.

This is very variable. The patient may complain of nothing, and the condition be found only by accident. On the other hand, there might be only slight displacement with a great deal of distress. As a rule, there is pain, mainly over the sacral region or lower back, or radiating down into the legs, mainly along the back of the thighs. A sense of weakness in the back is common. Movements of the back may be restricted in all directions, but in some cases are not limited at all. Spasm of the erectores spinae is common, and occasionally involvement of the nerve supply to the viscera, causes incontinence of urine and faeces. The latter are not common, however, due to the fact that the separation of the pedicles make a wider space for the nerves to leave the vertebral canal, and so they are not compressed.

On examination, the carriage is upright, and the shoulders thrown back. There is a prominence over the lower part of the back at the spine of the fifth lumbar, and above this a deep groove where the column is displaced forwards. The hips are prominent and squared, "like those of a cow." The nates are hollowed laterally and narrow. The costal margin is close to the iliac crests. The abdomen may be creased transversely, due to the shortening of the torso. On the whole, the body appears unusually short for the height of the patient.

Vaginal examination may show the true conjugate to be unusually short, due to the encroachment of the fifth lumbar vertebra upon the inlet of the pelvis. The gait may become a waddle. Also the intertrochanteric diameter may be so altered by a rotation of the femora, due to the new position of the pelvis, that it is shorter than the intercristal, whereas in the normal, it is greater than the intercristal. The diagnosis may not be made until X-ray plates have been taken. Although the anterior-posterior view may show the condition, lateral plates are more reliable and should show it up without any doubt. They show that the alignment of the anterior surfaces of the vertebrae is broken at the point of dislocation.

Treatment.

Restoration of the normal bony conformity is not possible although this would be the ideal method. Attempts at this have been made by means of suspension, and traction, but with little effect. However, excellent symptomatic results are obtained by means of spinal fusion, and this treatment has become the standard. The rationale of this is that it first puts at rest the bony surfaces that were formerly rubbing and thus setting up an inflammation, and thereby relieves the pain that such inflammation might have caused. Further, it so bridges the sacrum to the lower three or four vertebrae that all strain is taken off the ligaments about the damaged vertebra, and they also are put at rest and so the pain caused from that source is relieved. The slight amount of limitation that results from the fusion of the lower part of the spinal column is insignificant. Frequently the results of such treatment are dramatic.

The actual technique of the operation does not much matter, for excellent results have been obtained by all the customary fusion operations. Hibbs method, Albees operation, and the bilateral pedicle graft are commonly employed as in other spinal afflictions. Campbell devised an operation to fuse

the transverse processes of the fifth lumbar vertebra to the iliac crests and so hold the dsplaced body firmly to the ilia. Burns of Cambridge also performed a successful fusion of the fifth lumbar body to the body of the sacrum by means of an abdominal approach. He drilled a hole through the fifth lumbar body into the first sacral body, through the intervertebral interval, and then drove a tibial peg in through this. The graft successfully fused the adjacent vertebra and prevented further dislocation, and relieved symptoms. This has also been done successfully in Toronto.

Etiology.

From the time of the earliest observations of the condition the etiology has been a matter of dispute. It has been generally held by some that it is traumatic in origin, and by others that it is due to a congenital defect in the laminae of the affected vertebra that permits the separation of the arch. It is not possible to add anything to what has already been noted in regard to these theories by others. The following remarks will indicate, however, that probably there is reason in both beliefs. Firstly, there has been at least one case of a congenital spondylolisthesis recorded in a full term infant that died at childbirth, and in which there was no history of trauma to account for the condition. This was recorded by Blume in 1933. Also other cases have been recorded in children in whom it is not possible to get conclusive evidence that there was any trauma to cause it. In support of this congenital theory also there is the fact that there is seldom callus or any other evidence of fracture or injury to explain it on a traumatic basis. In addition the true congenital case above reported showed a failure of the normal bony centres to develop in the region of the pedicles, which, had the child lived, would certainly have been evident later as a defect in the pedicles such as is believed to be the actual cause of spondylolisthesis in adults. Further, many cases at autopsy and under the X-ray show a defect in the arch in the region of the pedicles that do not show any spondylolisthesis, and these are considered to be potential cases by many.

On the other hand it is argued by others that the condition is traumatic for the following reasons: Firstly, since there are found frequent defects in the region of the pedicles, why is the incidence of spondylolisthesis not more common if this is the main reason for its occurrence? Also, although certainly all the cases do not show callus and other signs of fracture, some of them do, which is evidence of injury. In addition a great many of the patients relate the onset of symptoms to some definite traumatic occurrence, where they had no symptoms previously. In addition even where there is not such definite history of trauma it is argued that the trauma might be mild in degree, but exerted over a long time, and it is only when there is some other factor acting with it that it leads to an actual sponlylolisthesis, e.g., the softening of the pelvic ligaments in pregnancy. In only 50% of cases is there any definite history of trauma, however.

It would seem, therefore, that though there might be either a true congenital form of the spondylolisthesis, or a true traumatic form, probably both these factors come into play in the development of most of the cases. At any rate the factor of a congenital defect is considered so important by some that they advise that a fusion operation be done in any case where such is found by X-ray or at operation.

Finally, no matter what the etiology, the anatomical deformity is one that lends itself in most cases to surgical interference most satisfactorily as far as functional results are concerned. For this reason one should not hesitate to advise a fusion operation in any case in which the condition is proven by X-ray, and there are any symptoms attributable to it, providing

there are no contraindications to operation.

Summary.

1. Sponylolisthesis was defined.
2. Historical note.
3. The pathology of the condition was described. This is primarily a separation of the vertebral arch at the pedicles. But this local abnormality brings in its train a series of abnormalities that affects the bony conformity of the whole spinal column and the pelvis.
4. The symptomatology was outlined. This is variable but usually permits a tentative diagnosis to be made, which should always be confirmed by X-ray. The X-ray findings are necessary for a sure diagnosis, and should rule out other conditions that might be confusing clinically.
5. Treatment. In the ineffectuality of attempts to restore normal anatomical contour, the treatment is to fix the parts in their present condition. This is attained by spinal fusion of the lower three or four lumbar vertebrae to the sacrum. This as a rule brings about an excellent functional result.
6. The etiology was discussed, and the conclusion reached that although there might be either true congenital forms from a congenital defect in the pedicles of the vertebral arch, or a true traumatic form, probably most of the cases are a result of a combination of both trauma and a congenital factor.

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THE FUNCTIONS OF THE SPLEEN IN HEALTH

By K. J. R. WIGHTMAN, '37.

In dealing with this somewhat difficult subject, it is my intention to preface the discussion of function with a brief outline of the anatomy of the organ, as I feel that it adds greatly to the ease with which the function of the organ may be understood. A good deal of our knowledge of the spleen has been arrived at in a more or less inductive fashion. Experimental studies are rendered somewhat difficult by the fact that its tissues are not peculiar to the organ, but find representation in many other parts of the body, and these accessories may readily assume functions which may normally be carried out in the spleen. Since the organ is of the nature of a ductless gland, the chief experimental approach has consisted in observing results after its removal. Early workers did this, and were disappointed to find no change, so that they were left with the opportunity of theorizing on its functions. Fortunately, modern experimental methods appear to have relieved us of this necessity to some extent.

The spleen may be simply described as consisting of a fibro-muscular capsule, from which trabeculae containing blood vessels pass into the interior. These act as a framework, in the interstices between which is a cellular reticulum containing numerous blood channels and various cellular elements. The latter may be divided into two main classes, the lymphoid and reticulo-endothelial tissues, which, from their anatomical disposition and reaction in disease appear to be quite distinct in function. The lymphoid tissue is massed in typical follicles, which surround the arterioles as they leave the trabeculae, forming an irregular cuff. These are the so-called Malpighian corpuscles, and are more prominent in the normal spleen in early life. The reticulo-endothelial cells form the basis of the so-called red pulp, consisting of a meshwork of flat, branching cells (the reticulum) which supports many large phagocytic cells, and through which course myriads of sinusoids, lined by these cells and containing blood.

The circulation of blood through the spleen is a problem which has interested many workers, and its importance is reflected by the fact that only through its blood supply is the spleen linked with the rest of the body. It was soon recognized that the spleen could and did hold variable amounts of blood, which meant that its arterial inflow did not necessarily parallel its venous outflow. This, coupled with the extreme histological complexity of the organ, excited a good deal of curiosity and some dispute. Two theories seemed possible—the first being that there was a two-fold circulation, the blood flowing through the spleen at rest being completely contained within endothelial channels (that is, closed.) But these channels had incomplete walls so that when the spleen became active, the blood in the pulp spaces could be included in the general circulation through the organ—or, in other words, the circulation would become open. This view is held by McNee and Barcroft, the former on the basis of injections of spores into the artery of a perfused spleen with the finding that they appeared to pass directly from the arterioles into venules. The latter supports his views on the basis of his well-known carbon monoxide experiments, in which he found that the splenic blood of an animal inhaling various concentratons of carbon monoxide, did not contain the gas until 20 minutes or so after the general arterial blood showed its presence—providing that the animal was at rest. If, however, the animal

were made to exercise, the blood in the pulp spaces became impregnated with the gas as rapidly as the arterial blood. Then, allowing these animals to rest in pure air, he found that the splenic blood freed itself much more slowly from the gas than did the systemic blood. These findings do illustrate that the circulation of the spleen is different at rest and during exercise, but recent work by Dr. Robinson indicates that the mechanism ascribed by these workers is not the correct one. He describes the circulation as follows: The splenic artery breaks up into branches, which travel in the trabeculae, from which non-anastomotic branches pass out into the pulp, where they are surrounded by a more or less irregular cuff of lymphoid tissue. End branches emerge from this to enter a more or less globoid mass of cells, the so-called ellipsoid. Here the arteriole, as a complete structure, ends, although an incomplete endothelial tube may be continued a short distance past this, either to fade away imperceptibly into the pulp spaces, or to end in a definite larger pulp space—named the ampulla by Thom. The ellipsoid is made up of plump reticulo-endothelial cells, more closely packed, and with shorter processes than those in the pulp. It marks the first contact of the blood with phagocytic elements, and its intercellular spaces are in direct continuity with the pulp spaces, albeit somewhat narrower. The venous collecting system is completely separate. It begins in the pulp as a widespread network of incomplete endothelial tubes, which are brought into continuity with the pulp spaces through stomata in their walls. These enter the trabeculae and unite to form typical veins with complete walls, which carry blood via the portal vein to the liver. It is thus possible to inject the pulp by forcing substances into either the vein or the artery, but it has not proved possible to inject the arterioles by forcing substances through the veins — a fact which led some investigators to suppose that the ellipsoid had a valve-like action, preventing regurgitation of blood into the artery when the pulp was compressed. The veins are so related to the trabeculae that when the muscular elements contract, compressing the pulp, the veins walls are held widely open, so allowing the blood to be forced out of the pulp spaces.

To summarize, therefore, we have in the spleen a siding in the general circulation of variable capacity, in which blood flows through spaces lined by reticulo-endothelial cells and in close relation to lymphoid aggregations.

Its Functions.

The first function that suggests itself is that subserved by the muscular tissue. Barcroft has demonstrated in a series of ingenious experiments with cats and dogs that the spleen as found after death, is only one-third to one-quarter the size of the living organ, and that the living spleen can respond to various stimuli by quite rapid contractions. By this means, it is able to expel a volume of blood which is equal to about one-sixth the total blood volume, but which contains far more red blood cells than the normal blood, its haemoglobin being on an average 120%, and going up to 140%. This means that about one-quarter of the total number of red cells may be stored in the spleen and expelled on demand. The cat spleen is more muscular than the human spleen, so that the function is somewhat less efficient in the human. The spleen may contract reflexly, through the splanchnic nerves, or by humoral mechanisms, notably by adrenalin and pituitrin. It is believed that the function is controlled from centres in the hypothalamus, which are influenced by the pressure, oxygenation and temperature of the blood supplying them, as well as by various reflex and higher nervous influences. Thus contraction of the spleen, with emptying of the pulp spaces, occurs during exercise, emotion, anoxemia from any cause, haemorrhage and higher environmental temperature. It is, therefore, an important adjunct

to the circulation, providing it with a large and readily available reserve of blood. Its importance was illustrated by Barcroft's CO experiments, as he showed that splenectomized animals succumbed to exposure to the gas more rapidly than the controls. He suggests, therefore, that the possession of a spleen may determine the survival of an animal in any emergency where life depends on the available supply of haemoglobin. This appears to be the only function which can be considered as peculiar to the spleen.

The disposition of the reticulo endothelial elements suggests a further function of filtration. That this does occur has been amply demonstrated by experimental injections of numerous colloidal substances through the perfused spleen, and by histological investigation of the spleen post mortem. Dr. Robinson's experiments indicate that the mechanism of filtration does not depend upon the minuteness of the pores through which the blood passes, but rather upon the existance of a Helmholtz double layer, or electrical potential on the surface of the cells, which is such that all electro negative particles coming in contact with them are adsorbed to their surface and can be dislodged only with difficulty. This function does not depend upon the vitality of the cells. The main requirement is that the particles come in direct contact with the cells—which is facilitated by the extreme tortuosity of the blood channels, and the immense surface area of the branching reticuloendothelial cells. The ellipsoids, with their narrower spaces and strategic location appear to be the main centres for this action. Carey has shown that pigment arrested in the ellipsoids in the injection of India Ink into animals tends to be transferred into the pulp spaces after a time—he suggests that the cells containing it migrate away from the ellipsoid and a proliferation of remaining cells occurs to take their place. Once adsorbed, these particles are phagocytized, through the action of another set of forces which appears to depend upon the vitality of the cell. At any rate they are permanently removed from the blood stream. The main impurities normally removed by the spleen are fragments of red blood cells and bacteria, with others of doubtful or lesser importance.

The removal of red blood cells—the so-called grave-yard function—has been shown to occur in the bone marrow to a great extent. Hepatectomized animals are reported to become jaundiced as rapidly when they are also splenectomized as when they are not. The mechanism of blood destruction is described by Rous as consisting of a preliminary fragmentation in the circulation, with phagocytosis of the fragments in the spleen, bone marrow and liver. The phagocytosis of whole erythrocytes is not believed to occur normally. One possibility which exists in this connection, is that the spleen may have something to do with the fragmentation. It has been shown that the red cells are more resistant to haemolysis after splenectomy, so that the spleen may prepare the cells for their ultimate break-down. This is suggested by Bottazzini in his haemocatatonistic theory. The haemoglobin is broken down into bilirubin—which is carried to the liver in the blood—and an iron-containing fraction, which appears to be stored in the cells, later to be used in the manufacture of new haemoglobin. The bilirubin is excreted by the liver, and would thus be expected not to appear in the systemic blood. Nevertheless, it appears to be easier to produce jaundice in animals with spleens than when splenectomized, apart altogether from the haemocatatonistic action of the spleen described above. In the splenectomized animal the break-down of haemoglobin occurs in the bone marrow and liver, so that the main part of the bilirubin formed is discharged into the systemic blood, where it is suggested that it is much more dilute than in the portal blood of an animal with a spleen—and so the liver

can excrete it more efficiently. However, this alone does not appear to explain the fact.

The removal of bacteria from the blood as shown by Wyssokowich and later studied in more detail by Bull, occurs mainly in the spleen and to a lesser extent in the bone marrow, liver and lymph glands. Thus the spleen, together with the rest of the reticulo-endothelial system, might be expected to be an important factor in resistance against disease. In addition to phagocytic powers, there is some evidence that the spleen also exerts an antigenic function, both by virtue of its lymphatic and reticulo-endothelial cells. Jelin showed the importance of the spleen in resistance in rabbits to typhoid and other saprophytes. Luckhart and Becht showed that the spleen can partly fix antigens, and that in the absence of the spleen the dog cannot produce haemolysins, haemagglutinins or haemopsonins as rapidly. Morris and Bullock showed that rats were rendered much less resistant to plague by splenectomy. A rather peculiar dispute has arisen regarding the effect of splenectomy on resistance to tuberculosis. One set of workers found the resistance to tuberculosis increased after splenectomy. Murphy and Ellis claim that they waited too long after splenectomy before innoculating their animals, and by innoculating their animals shortly after splenectomy, showed resistance is lowered. They claim that the previous workers had allowed sufficient time to elapse for compensatory hyperplasia of the lymphoid tissues to occur. While this is not very conclusive, it does demonstrate the experimental diffculties to be overcome.

The relation of the spleen to haematopoiesis is another vexing problem. It has been shown that it plays a direct part in this in the fetus in so far as it produces red blood cells, polymorphs, lymphocytes and monocytes, and can apparently revert to its fetal state under some circumstances. In the normal adult, however, it only produces lymphocytes and probably monocytes. However, the results of splenectomy suggest that it also has an indirect action on this function. After splenectomy a marked change in the blood picture occurs in most animals, and in the human. The red blood count is reduced by a million or two, the red blood cells are seen to be poor in haemoglobin and the reticulocyte count goes up. In humans, but not in animals, nucleated forms make their appearance. The haemoglobin seldom goes down below 55%. In addition to these findings, the white blood count is up, the platelet count is up. At the end of two months or so these changes are all gone, and a relative lymphocytosis and eosinophilia remains. On examining an animal after recovery from this anemia, one finds that the bone marrow is quite hyperplastic, with transformation of the fatty marrow into red marrow. There is also evidence of lymphoid hyperplasia. This apparently paradoxical response to the removal of a blood-destroying organ has been explained several ways. Krumbhaar suggests that it is due to the loss of a splenic hormone which normally stimulates the bone marrow to increased haemopoiesis. He supports this view by showing that injection of splenic extracts will relieve this anemia. The anemia appears to be aplastic in type rather than haemolytic. It disappears spontaneously when the reticulo-endothelial tissues of the bone marrow have undergone compensatory hypertrophy. He found that the anemia occurred when an Eck fistula was made, or when the splenic vein is transplanted into the vena cavo. This would suggest that the liver was also active in the production or modification of the hormone. Other workers suggest that this hormone is formed from break-down products of the erythrocytes. It would appear difficult to imagine why the myeloid system of leucocytes should be stimulated, when

the erythropoietic tissues are depressed. A diet rich in iron does not relieve this anemia.

An interesting reflection on this work is provided by the discovery of Bartonella (virus) infections in rats, and lately in dogs and rabbits. This infection is apparently latent, and becomes unmasked when the spleen is removed, producing an anemia which is practically identical with that described as occurring after splenectomy. This, too, is recovered from spontaneously as the compensatory hyperplasia develops. While it is difficult to say how this affects our evaluation of Krumbhaar's results, and those of others, it does illustrate the importance of the spleen in immunity.

It should be mentioned that some observers have found a polycythemia after splenectomy and postulate an inhibitory effect on erythropoiesis for the spleen, this being further substantiated by the appearance of Howel-Jolly bodies, which these men have observed. Krumbhaar replies that these effects are transitory and post-operative, and fails altogether to find the Howel-Jolly bodies. The answer to the problem is still to be found.

Leaving this subject, we come next to the influence of the spleen on metabolism. Findings in this field have been essentially negative with the exception in regard to the metabolism of iron, cholesterol, and bile pigment. The basal metabolism and nitrogen balance are not significantly changed.

The relationship of the spleen to iron metabolism is tied up with the destruction of erythrocytes, since this forms the source of all the iron in the spleen. The organ is rich in iron which is stored here and in the liver in a simple inorganic state. Lintzell and Radeff claim to have shown that the liver and spleen iron content maintain a constant ratio to one another in definite states of the circulation, and that the total iron content of the blood, liver and spleen tends to be a constant under all conditions. Sandberg and Perla report that the iron is retained for four weeks after splenectomy, and that copper begins to be excreted after two weeks. On the other hand we have the work of Krumbhaar and Wilson using dogs on a carefully controlled diet. They report a slight increase in iron excretion which lasts as long as the anemia. They suggest that it may have a part in causing the anemia, rather than being caused by the anemia. So here again we have the marshalling of authorities on the two sides of the question. One thing quoted in Krumbhaar's earlier article is that injection of electro-ferrol does not relieve the anemia after splenectomy. However, the removal of the spleen must at least influence the course of iron metabolism, whatever effect it may have on iron balance, which appears to be readily duplicated by the hypertrophied bone marrow.

The cholesterol content of the blood stream after splenectomy appears to vary, as does the level of unsaturated fatty acids. Whether these factors are directly concerned with the removal of the spleen, or whether they depend on the effect splenectomy has on the liver is difficult to say. The most clear cut results of splenectomy occur in those types of anemia where the blood cholesterol tends to be high. Splenectomy will bring the cholesterol level back to normal. This has led some workers to believe that the spleen has a cholesterogenic function in these diseases, and probably in health. This matter, like most others concerning the spleen, is not settled. The utilization of ordinary fat does not appear to be altered.

Turning now to a subject which should perhaps have been mentioned under the heading of immunity, we observe the marked resistance that the spleen shows to malignant tumours. Although gross secondaries in the spleen are rare, Kittle reports that microscopic secondaries may be common-

ly found if large sections of the organ are studied. Experimental work with tumour grafts show that these rarely take in the spleen and that grafts planted in the skin together with spleen tissue grew much less rapidly than those planted with other organs. Some observers report that splenectomized animals showed a lower resistance to tumour growth—and as one begins to expect, others find that it makes little difference. This resistance is probably concerned with the phagocytic powers of reticuloendothelial cells which in the spleen prevent local growth of tumour and quite possibly prevent tumour growth elsewhere by splenic action on the reticulo-endothelial cells of that region.

And finally we come to the relationship of the spleen to other organs. Naturally, removal of one organ is almost expected to cause changes in the action of others, but experiment shows that there are special relationships between the spleen and other organs. To summarize, a definite relationship between the spleen and liver exists mainly as concerns acetone formation and the production of haemolytic agents. It exerts a definite action on calcium metabolism, synergising with the parathyroid bodies. A relation to the thymus, pancreas and ovary has been suggested, but there is little to substantiate it.

In closing, I feel that some explanation of the extraordinary experimental discrepancies should be attempted. The fact that the spleen is not alone in the possession of lymphoid and reticulo-endothelial tissues, that its loss is rapidly compensated by other representatives of these systems, all conspire to make the results of splenectomy ambiguous unless most carefully controlled. Add to these the differences in relative size and structure of the spleen in different animals, and the extreme variability of most of the bodily functions observed, and the confusion is twice compounded. I can only hope that I have been able to give some clear conception of the possibilities which exist.

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THE FUNCTIONS OF THE SPLEEN IN DISEASE

By HENRY F. SAUNDERS, '36.

The spleen is a hemolymph gland and as such it belongs to the reticulo-endothelial system. As it is only a part of this system, its removal causes little or no change in the functions of the body. Patholigically, however, is of extreme importance.

Under physiological conditions there is maintained a fine balance between bone marrow hematopoieses and the splenic function of cell storage and cell death. To express this Krumbhar proposed the term hemolytopoietic equilibrium. In medicine as soon as a physiological function is recognized for any organ, a disease entity due to a corresponding dysfunction may be anticipated.

In dealing with the subject of the functions of the spleen in disease, as it is manifestly impossible to deal with all the diseases of the spleen, only those conditions which we are likely to meet in wards of Toronto hospitals, will be considered.

McNee presented a classification of diseases of the spleen in 1931, which is probably the best suggested so far. This I shall use in a somewhat modified form. He classifies the disease of the spleen on the basis of histological changes, as they affect one or other of the different essential structural parts of the human spleen. Tumours and specific infections fall into their own special group. Hence our classification is :

1. Infections.
2. Diseases affecting myeloid and lymphatic elements.
3. Diseases affecting the reticulo-endothelial system.
4. Diseases affecting the vascular system.
5. Tumours.

In Infections.

In many infections such as typhoid, carditis, septicaemia, and others, the spleen may become palpable. In typhoid this is due to an enormous proliferation of the R.E. cells similar to that seen in Peyer's Patches, lymph nodes, etc., plus a massive engorgement of the pulp spaces with erythrocytes. Why the red blood cells accumulate and are broken down is not clear. Possibly they have become injured some way and are now being buried by the spleen. In septic conditions, the pulp is full of enormous numbers of polmorphonuclear leucocytes, myelocytes, and other oxidase positive cells, which are filtered out by the spleen for the circulation. Goldzier considers that here too, there is a R.E. cell hyperplasia.

Hence the spleen in acute infections filters out the degenerating blood cells and this no doubt is a means of removing from the circulation cells which are no longer of use in controlling the infection. Prof. Robinson was not able to convincingly prove that the spleen filtered out bacteria, but some consider that the spleen does do so and phagocytes them. The hyperplasia of the R.E. cells is considered to be an immunity reaction although definite proof of this is lacking.

Often the spleen becomes a habitat for bacteria and protozoa which it is unable to destroy and consequently gives rise to the re-infections so often seen in the splenomegalia of syphilis and malaria and tuberculosis, characterized by chronic anaemia and failure to respond to treatment. These cases are amenable to radical surgery.

Hodgkin's disease is a disease of the hemopoeitic system and is only considered here because it presents the clinician with a case of splenomegaly.

In 75% of cases of Hodgkins disease the spleen is enlarged and firm, with numerous opaque patches of grey or yellow scattered throughout it. The latter represents the areas of diseased tissue. The pathological physiology of the spleen in Hodgkin's is not known. Does the spleen become involved due to its filtration of metastatic emboli, or does the vague influence which initiates the disease affect the spleen similarly?

In Diseases of Myeloid and Lymphatic Elements.

When we come to the disease affecting the myeloid and the lymphatic elements we are dealing with generalized diseases involving the spleen. In this group we must consider the leukaemias.

In the myelogenous leukaemias the spleen is greatly enlarged and may fill the entire abodmen. It is dark in colour and infarcts are common due probably to the formation of leucocytic thrombi in the small vessels. The splenic pulp is crowded to capacity with myeloid cells of every description. This is probably due to the filtration from the blood and storage of many of the cells which are not necessary in the circulation. To some extent, too, the spleen may resume a fetal function and manufacture the myeloid cells from its primative mesenchymal cells. A similar picture is seen in the lymphatic leukaemias with the difference being that the lymphocytic type of cell rather than the myeloid variety is seen. Klemperer brings out the point that the relative size of the spleen is of very little diagnostic value in differentiating between myeloid and lymphatic leukaemias, and although it is true that the average weight of the spleen is far greater in the myeloid type than in the lymphatic, nevertheless, individual cases of lymphatic leukaemia not infrequently have very large spleens.

That the spleen on the one hand filters out and stores some of the excess of the myeloid and lymphatic cells in an attempt to maintain a normal level of these cells in the blood, and on the other hand attempts to manufacture more cells is just one of many things which we cannot explain.

In connection with the filtration and storing function of the spleen in an attempt to maintain Krumbhaar's hemolytopoietic equilibrium we may consider polycythaemia vera. In this condition there is an extreme hyperplasia of the marrow with a very high red count, high percentage of haemoglobin and an increased blood volume. In this disease, as we would expect, the spleen is enlarged, full of red cells and with signs of active phagocytosis. This, no doubt, is an attempt to maintain a normal level of erythocytes in the blood.

In Diseases of the Recticulo-Endothelial System.

Diseases affecting the endothelial elements of the R.E. system is the third group in McNee's classification. This group is divided into two divisions:

1. Hemolytic (Acholuric) Jaundice.
2. Disturbances of Lipoid Metabolism—which include Gaucher's Disease, Neimann-Pick's Disease, and Hypercholersterolaemic Splenomegaly.

Let us also consider under this group Werlhof's thrombocytopenic purpura.

Hemolytic Icterus may be described as a hemolytic disease with hemolytic crises and varying degrees of anaemia and acholuric jaundice, active regeneration of blood, splenomegaly, and increased fragility of red blood cells. Familial, congenital and acquired types have been described; however, little clinical and laboratory distinction can be made in most cases.

The spleens are not enormously enlarged, and have a characteristic histological structure quite distinct and unlike any other form of splenomegaly. The pulp spaces are seen to be engorged with red blood cells so numerous

that the actual structures of the organ can only be made out when the blood is allowed to empty from the organ before fixation. In the active stage much iron containing pigment is found in the R.E. cells of the pulp.

The jaundice is usually present continuously, with exacerbations and intermissions, from an early age—and in uncomplicated cases the blood serum gives the indirect Van den Bergh reaction. Severe crises may take place with increasing jaundice, enlargement of the spleen, fever, headache, nausea, epigastric distress, and sometimes vomiting. The anaemia is usually mild with evidence of active bone marrow regeneration — there may be 10-40% reticulocytes, polychromasia, and nucleated reds, microcytosis and spherocytosis is so definite and characteristic a feature of hemolytic icterus that a presumptive diagnosis can be made without any other data. The red blood cells hemolyse in between 0.7 - 0.45% saline solutions—(normal 0.45 - 0.35%).

That there is excessive hemolysis and destruction of the red blood cells seems very obvious. This might be accounted for by the following possibilities:

1. That the bone marrow produces abnormally fragile cells which easily fall prey to the normal phagocytic action of the R. E. cells.

2. That the cells produced by the marrow are normal, but that they are injured outside the bone-marrow, thus making them more fragile and easily hemolysed and phagocyted.

3. Due to the combination of these.

That the bone marrow does produce abnormally fragile cells seems likely. Noegeli and Haden have shown that the bone marrow in this disease produces abnormally small and thick red cells (i.e., a microcytosis and spherocytosis is present). The normal red cells, they note, undergoing hemolysis become thicker and globular and at a certain point hemolyse. In hemolytic jaundice at the very beginning the shape of the cells already corresponds to one of the stages through which a normal blood cell must pass when placed in hypotonic solutions and hence, the cells in this disease may be regarded as nearer the hemolysis point by reason of their shape. Hence these abnormal cells more easily become hemolysed and phagocyted. It is well known that in acholuric jaundice the lymph glands and pulp cells of the spleen, the Kupffer cells of the liver all have large deposits of iron-containing blood pigment. But, if the marrow is primarily the source of the trouble in hemolytic jaundice, why should splenectomy, which removes only a large portion of the reticulo-endothelial system, cause the alleviation of the signs and symptoms when other portions can hypertrophy and show marked hyperplasia? Obviously the spleen has some part to play other than that which its contained R.E. cells perform.

There is some evidence to show that the spleen influences bone-marrow hematopoiesis. It is recognized now that following splenectomy in acholuric jaundice the resistance of the erythrocytes reaches more normal limits. Pearse and Krumbhaar in 1929 showed that following splenectomy in normal animals and man the resistance of the erythrocytes to hypotonic saline and other hemolytic agents is increased. Not only does the spleen in normals (man and animals) affect the resistance of the erythrocytes but also following splenectomy there is more or less persistent leucocytosis, increase in the volume of active bone-marrow (noted only in animals), a hyperplasia of lymphoid tissue and an increase in the number of circulating platelets. All of which tend to prove the existence of an inhibitory action of the normal spleen on bone-morrow. Krumbhaar on the contrary still maintains his original thesis that the spleen stimulates bone-marrow which he interprets from the finding of a secondary anaemia in normal dogs following splenectomy.

The hyperplasia of the bone-marrow, however, is in excess of that necessary to overcome the secondary anaemia. In normal humans splenectomy does produce temporarily a slight anaemia. However, following splenectomy in acholuric jaundice the red count rises by half a million almost immediately. Krumbhaar agrees with this finding but states that the removal of any diseased spleen in acholuric jaundice is not the same as removing a normal spleen. The sudden rise in the red count post-operatively might be due to the expression from the splenic pulp of a large amount of red cells producing an auto-transfusion as suggested by Dameshek.

Minkowski was the first to suggest a primary increased hemolytic activity of the spleen. Hence the spleen, if this is true, is not only spodogenous, but actively destroys increased numbers of red cells. There are very few adherents to this thesis—that by the increased hemolytic activity of the spleen the pathogenesis of this disease is explained. Although it is not possible to demonstrate hemolysis in normal spleens, we cannot exclude the possibility that it exists and that it is active in some disease conditions. Some have advanced the theory that the serum in acholuric jaundice contains hemolysins, which hemolyse the red cells in the circulation, with the spleen and the rest of the reticulo-endothelial system merely acting as scavengers. That there are no autolysins is definitely known, but isolysins have been noted in some cases. Probably the occasional bad results following blood transfusions in these cases is due to the presence of these isolysins. However, that normal red cells are produced only to be injured by hemolysins in blood, is not the accepted explanation.

The general concensus of opinion is that both the marrow and the spleen are implicated in this disease, with the spleen playing the major rôle. Krumbhaar stated recently that he considers the spleen the major offender, but that the primary defect is in the red cells, because of their shape. He states that the spleen may acquire the rôle of chief offender from long practice in destroying the congenitally poor red cells.

Splenectomy in chronic hemolytic jaundice has been practised for many years and offers the best and practically only treatment. The rationale of splenectomy, when first started, was that splenectomy would remove a large part of the phagocytic reticula-endothlial system, and thus the fragile cells would have greater chance of survival. In a very few cases, the symtoms recurred, probably due to an accessory spleen not seen at operation. Splenectomy done on patients with active bone marrow, as evidenced by high percentage of reticulocytes, polychromasia and nucleated reds almost invariably leads to cure. Post operatively, the cells, as indicated above, show increased resistance and the evidence of increased bone-marrow activity disappears, indicating that lessened activity of the bone-marrow is sufficient now and jaundice disappears.

Contrary to all previous principles, Doan and his co-workers have in the last five years removed the spleen in the acute hemolytic crises with apparently immediate improvement of the patient and dramatic rise in red count. They believe that the spleen in hemolytic jaundice excessively destroys the circulating elements of the blood and exerts an undue inhibitory effect on bone-marrow hematopoiesis.

Disturbance of Lipoid Metabolism of the Reticulo-Endothelial System.—This rare group includes Gaucher's Disease, Niemann-Pick's Disease and the Hypercholesterolaemic Splenomegalies. In 1882, Coats of Glasgow discovered large cells full of lipoids in cases of diabetes mellitus with lipaemia. In 1914, Anitschkow experimentally produced, by feeding animals large quantities of cholesterol, large deposits of cholesterol esters in

the whole of the reticulo-endothelial system. It is believed now that in this group this system is only secondarily involved in a disturbed lipoid metabolism. The lipoids are not identical, but are similar. What exactly is wrong with the fat metabolism is not known, but we do know that the whole system is hyperplastic and hypertrophied, probably in an attempt to remove from the circulation the abnormal products of fat metabolism.

Thrombocytopenic purpura or Werlhof's purpura is an acquired hemorrhagic disease of unknown origin. It is characterized by hemorrhages, and may be of a chronic remittent type lasting 10-15 years, or severe in nature lasting 1-4 weeks. The hemorrhages may be of any degree, and are either spontaneous or traumatic. This is not a familial disease. The spleen is moderately enlarged, but may not be palpable at all. Certain features of the blood are important from a diagnostic standpoint. The platelets are markedly diminished, even below 60,000. The bleeding time, normally 1-2 minutes, is prolonged to 10-20 minutes. There is a normal coagulation time (5-10 minutes), but a marked delay in retraction of the clot.

Since the main pathological lesion existing in the thrombocytopenia and since the severity of the bleeding bears a close relationship to the number of platelets, we readly assume that the thrombocytopenia is responsible for the occurrence of the haemorrhage. But it has been noted in severe cases that the bleeding may cease several days before the platelet count rises and the platelets have been known to disappear without the production of hemorrhage. Bedson experimentally produced by injection of agar intravenously, a greatly reduced platelet count without the production of hemorrhage. He also produced a hemorrhagic diathesis in animals as well as in man, by the injection of a specific platelet anti-serum. This reduces the platelet count, but he considers it injures the capillary endothelium as well. This has been borne out by histological studies, which show swollen and oedematous changes in the capillary wall. Hence Bedson claims that two factors are necessary to produce hemorrhages. (1) Capillary endothelium damage, which is of prime importance, and (2) diminished platelets. If the endothelium was damaged and sufficient platelets were present, they would patch up the weakened wall and no hemorrhage would result, but if the capillary endothelium was damaged extensively enough, and if there was a relative insufficiency of platelets, hemorrhage would result. Recently Bemelmans claims that a streptococcus toxin plays some part in capillary injury. This seems to be an excellent suggestion, because many have noted the diminution and sometimes disappearance of symptoms after the removal of foci of infection. Mild recurrences have occurred in some of the cases after the elimination of foci infection.

When the spleen was first blamed for the production of this condition, it was believed that the reticulo-endothelial cells, which normally phagocytize platelets, were doing this excessively, or else the spleen was inhibiting the platelet production as originally suggested by Frank. On these grounds, it was thought that splenectomy was indicated. This was done and although the hypothesis is probably incorrect in the light of recent work, yet following operation, there is an immediate cessation of hemorrhage and a rapid rise in the number of platelets. This increase in platelets may be the cause of the arrested hemorrhage. Recently Evans, Shore and Kreidel and others have studied the platelets after the removal of the normal spleen. They state that for three days the platelets remained at normal levels and then rose quickly to over one and a half million in 12 days, and then in five days returned to normal. This type of curve has been noted in other surgical procedures. with all types of anaesthesia, even local, and

even after trauma. Hemorrhage and anaesthesia by themselves do not affect platelets. The conclusion is that the rise is due to absorption of toxic products from injured tissue affecting a normal marrow. In Werlhof's purpura, the platelet rise after splenectomy is similar, only the onset is immediate and the maximum rise is reached in seven days. However, it has been noted that the platelets may fall to their original low level, in months or years without recurrence of clinical symptoms. Acute cases were formerly not subjected to splenectomy. Recently this has been done by Doan and others at Mayo with success. Hence to explain the hemorrhages, the blood characteristics, and the cure following splenectomy is in the light of our present knowledge, very difficult.

In Diseases of the Vascular System.—In this group we will consider briefly infarctions, Banti's disease, and the splenomegaly associated with hepatic cirrhosis.

Infarcts are frequent, because, as already explained, each of the main branches of the splenic artery are end arteries, in the truest sense and supply a potential splenic lobule. Total infarcts may occur following torsion of the pedicle of the spleen. Experimental tying off of the splenic artery does not lead to infarction, but rather an atrophy. McNee considers that infarcts only occur with an added factor, such as splenic disease itself or abnormalities in the distribution of the blood vascular system. Others state that anastomotic circulation at the hilus prevents infarction.

Banti's Disease.—In 1866, Gretsel defined a syndrome, which Gessinger termed "splenic anaemia." Many distinct disease entities have been separated from this general disease, such as Gaucher's, von Jaksch's, etc. In 1894, Banti described the disease which bears his name.

He divided this disease clinically into three stages:

1. A period lasting 3-12 years, characterized by splenomegaly with anaemia.

2. A short period lasting 12-18 months, characterized by swelling of the liver.

3. A final period, lasting 1-2 years, characterized by a small cirrhotic liver and ascites. In this stage, according to Banti, the symptoms are identical with any case of atrophic or portal cirrhosis.

In addition, hemorrhage from mouth and bowel, jaundice, and a secondary anaemia, with leucopoenia, are present. Death is invariably due to hemorrhage or intoxication from the cirrhosis. The disease is of unknown etiology, and the most common causes of splenomegaly, such as alcohol and syphilis, play no rôle whatsover.

The pathology consists of:

1. In the spleen, there is fibrosis of the reticulum and capsule, with narrowing of the splenic veins.

2. Fibrosis of the Malpighian follicles beginning around the central artery and proceeding outward. These changes Banti named "fibro-adenie." Osler, in discussing nomenclature, said that Banti disease is a chronic splenic anaemia, characterized by primary splenomegaly of unknown cause; a marked tendency to hemorrhage; in a few cases, a terminal stage ,with cirrhosis of liver, jaundice and acites—the latter when present make the diagnosis Banti's disease, because, despite the increase in connective tissue, the spleen still retained its glandular appearance. There is no evidence of blood destruction. Very few cases show this typical feature.

3. A cirrhosis of the liver is present, differing in no way from the ordinary atrophic or portal cirrhosis. Later Banti included in this disease those cases with typical clinical course and which an autopsy had no cirrhosis. He considered these cases to be in the first stage. With this inclusion, Banti's disease becomes synonymous with "splenic anaemia."

4. In many cases, there is an endo-

phlebitis and often calcification of the splenic and even the portal vein.

In 1910, Banti stated that the patholgy was not pathognomonic and lesions similar to those in Banti's disease have been described in malaria, tuberculosis of various serous civities, persistent umbilical vein, cirrhosis of the liver of various types and many others.

Banti believed that the pathogenesis of the disease was as follows: There was a primary splenomegaly, due to an infective agent. The enlargement of the organ produced in turn a splenotoxin, which caused a secondary cirrhosis of the liver and the changes in the veins. The anaemia was due partly to the hemorrhages and partly to the toxaemia.

Banti believed that the splenomegaly was primary, because of the large size of the spleen when the anaemia was not marked, the "fibro-adenie" of the spleen antedated the cirrhosis, and the cures obtained by splenectomy.

McNee, in 1931, says, in regard to the pathogenesis of Banti's disease that the whole problem is bound up with some disturbance in portal vascular system. He points to the frequency of the lesions in the veins and to the peri-ellipsoidal hemorrhages with nodular siderosis as evidence in favour of this. Nevertheless, he does not leave out the possibility that a toxin may be the etiological factor.

Peri-ellipsoidal hemorrhages and nodular siderosis is not specific of any one disease, and is found in Banti's disease, hemolytic jaundice, portal cirrhosis, leukaemias, and many others.

The siderotic nodules appear as yellowish-brown flecks, like flakes of tobacco-leaf. Microscopically, they present a peculiar filamentous appearance and have been mistaken for the mycelia of fungi. The filaments are merely elastic fibers on which have been encrusted iron crystals. With these filaments there are masses of hemosiderin and giant cells, the whole forming the siderotic nodule. These nodules are probably caused by hemorrhage at the point of termination of the ellipsoid, where there is a valvular arrangement so that raised portal pressure may cause rupture of the vessel at this point (McNee).

The changes in the veins have been noted by many, in many instances with thrombosis. Is Banti's view correct or is the splenomegally secondary to lesions in the veins? Warthin experimentally ligated the splenic vein in dogs and only produced an atrophy.

Larrabee says that even with the increased fibrosis, due to the increase in size of the spleen, there is an absolute increase in the number of pulp cells producing a hypersplenism, leading to an increased inhibitory action on the marrow and thus causing the anaemia. Hemorrhage and possible infection are additional factors in the production of the anaemia.

In 1925, Rosenthal noted that by using the platelet count in cases that he followed after splenectomy cases of Banti's syndrome could be divided into two groups:

(1) Thrombocytopenic group. — In this group, the blood platelets were low before operation, rose afterwards and fell to normal. These cases had a marked hemorrhagic tendency, but all were cured.

(2) Thrombocythemic group — in which the blood platelets were normal, but rose rapidly to high figures, after splenectomy and the increase persisted for months or years. These cases all developed thrombosis in the portal system and in the periphery, some of which were fatal.

Hence, pre-operatively all cases should have a platelet count done before attempting prognosis and treatment.

The hemorrhagic tendency in splenic anaemias may be due to two factors:

(a) Mechanical factor, probably related to the venous obstruction, due to cirrhosis or thrombosis, leading to en-

gorged vasa brevia, and oesophageal veins.

(b) Associated with the general hemorrhagic tendency, which may be correlated with deficiency of platelets. Such patients are good operative risks and prospect for permanent cure is good.

In considering the treatment for Banti's syndrome, Moynham states that splenectomy should be done as soon as the diagnosis is made. In early cases, the anaemia disappears, and a large percentage are cured. He says, too, that the operation in late cases is dangerous, due to the presence of adhesions and that it will not prevent the advance of the cirrhosis and the patients usually die of recurrence of hemorrhages. Occasionally a spectacular cure results, hence the patients should not be denied the operation. Sometimes the patient, though not cured, is made more comfortable, his ascites goes down temporarily, probably due to the diminished portal flow after splenectomy. Other methods, such as tying the splenic artery and X-ray treatment, are employed. The tying of the splenic artery, followed by atrophy, is a method of some use when the spleen is difficult to remove.

Let us briefly consider now the splenomegaly associated with hepatic cirrhosis. In 1907, Herrick perfused cirrhotic livers by way of the hepatic artery, at autopsy, and found that a larger proportion of fluid passed out the portal vein in the cirrhotic than in normal livers. He concluded that there is a freer communication between the hepatic artery and portal vein in cirrhotic livers and this must heighten the pressure in the portal vein. These findings are equally well explained by assuming that in cirrhotic livers, there is a greater obstruction to the passage of fluid through the hepatic lobule to the hepatic vein.

The splenic enlargement in portal cirrhosis may be due to: (a) Passive congestion, due to increased portal pressure—but this theory is inadequate, because the spleen occasionally is enlarged before the cirrhosis of the liver is at all advanced, and also the spleen is enlarged before any ascites or other definite signs of portal back pressure supervenes; also in only 80% of cases of cirrhosis is the spleen enlarged at all.

(b) A toxin circulating in the blood and reaching the spleen by its artery. McNee, in 1932, favoured this theory, because he points to Banti's syndrome, in which there is a primary splenic enlargement before any hepatic cirrhosis. What this toxic product is, we do not know.

The spleen in hepatic cirrhosis is not very large, but sometimes it may be enormous. With small enlargement of the spleen, the heightened pressure in the portal system is sufficient to account for its increase in size.

In cases which do not fit Banti's description, it seems advisable to describe the disease by the term spleen-liver syndrome, when spleen is more involved and by the term liver-spleen syndrome, when the liver is mostly involved and thus avoid confusion.

In Tumors.—The subject of tumors can be dismissed by saying that simple tumors are rare, as are malignant ones. The latter when present, are always sarcomata.

Finally, in the words of Galen, "the spleen is an organ of mystery in its diseases, functions, and metabolic activities." It is only when our knowledge of splenic function is increased that we may expect to correlate disordered function with bodily disorders, which we recognize by clinical symptoms."

WATER BALANCE

By R. W. I. URQUHART, M.A., M.D.
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Water is of the utmost importance in the animal economy, constituting as it does more than 70% of protoplasm. It is fundamental to all physiological processes and to life itself. Animals living under conditions limiting the supply of water are provided with special mechanisms to conserve or store water. The loss to man of 10% of his water content is serious to health and the loss of 20% results in death. It occupies a mid-position between food and oxygen in relation to duration of life.

The various physiological processes in the body are possible only because of the variety of properties water displays in relation to substances brought into contact with it, such as, solvent power, ionization, hydration, imbition, lubrication, etc. It is admirably adapted for heat regulation, since it is readily shifted to meet the rapidly changing needs of the body. It has a high specific heat, a high caloric requirement for evaporation and a high heat conductivity. It, therefore, favours storage of heat, permits of rapid elimination of heat and a rapid equalization of heat throughout the body.

It is essential, therefore, that adequate amounts of water be maintained in the body. This depends not only upon the total intake and output of water, the water balance, but also upon the proper functioning of a variety of mechanisms, for the most part concerned with its conservation to the body. For example, more water enters the gastrointestinal tract via the secretions than by the mouth. These secretions are re-absorbed and the water used over and over again, very little being finally lost to the body. In man, approximately 10 litres of water daily may be excreted into the gastrointestinal tract by way of the saliva, gastric juice, etc., and of this not more than 300 cc. are lost in the stools. This mechanism is an example of the so-called "intermediate water exchange."

Water balance may be defined as the daily relation between the total amount of water entering the organism through the ingestion of liquids and food, including the water of oxidation, and the total output of water by way of the kidney, bowel, lungs and skin. A rough clinical balance is often obtained by measuring the fluid intake and the urine output. This is, of course, grossly inaccurate. More accurate and comprehensive studies of water balance have been made by Atwater and Benedict, Benedict and Carpenter, and Dubois using the closed calorimeter.

From such studies it has been shown that the water intake is derived not only from the water ingested as such or in beverages, but also from the water contained in the so-called solid foods, many of which contain from 70-95% water. A further amount is supplied by the water of oxidation, that is, water liberated by the oxidation of organic matter in the cells, or by other chemical processes in tissue involving changes in molecular structure. 100 grams of fat give 107.1 gms. water of oxidation, 100 gms. starch give 55.5 gms. water, 100 gms. protein give 41.3 gms. of water. The ordinary mixed diet provides about 300 gms. water of oxidation daily.

The water output occurs by way of the kidney, bowel, lungs and skin. No definite rule can be laid down as to the amount of loss through any channel. Generally speaking, the loss in the feces is the least amount and the most constant. It amounts to about 300 cc. per day. The loss through the skin as sweat is subject to the greatest variation, but

on the average amounts to about 500 cc. per day. The loss by way of the lungs is a continuous loss, subject to much less variation and amounts to about 400 cc. daily. The kidney ordinarily excretes the difference between the total water intake plus the water of oxidation and the loss through skin, lungs, and bowels and is thus of the greatest importance in maintaining the water balance.

Water is stored in the intracellular and interstitial fluids of the body. Changes in water content of the tissues take place through the blood stream and apparently every effort is made to maintain the blood volume at a fairly constant level. Changes in water balance may result in one of two conditions, namely, dehydration or oedema.

Dehydration occurs when the amount of water lost to the body exceeds the amount of water ingested plus the water of metabolism. This water loss ordinarily results in decreased water content of the tissues. If sufficiently severe, it may also result in decreased water content of the blood and the condition of anhydraemia is said to be present.

Experimentally, dehydration may be produced by restricting water intake, or by increasing water output or by combining decreased water intake with increased water output. Clinically, dehyration occurs in a number of conditions which may be classified as to the means of water loss.

1. Undetermined—fever and infections.
2. Bowel — Asiatic cholera, diarrhoea, intestinal intoxication.
3. Skin—miner's cramp.
4. Gastric mucous membrane—upper intestinal obstruction, vomiting of pregnancy, gastric tetany, etc.

In both experimental and clinical dehydration, thirst is the first evidence of water deprivation. This is followed by a series of changes, the severity of which depends on the rapidity with which dehydration occurs. If the water loss is gradual, the blood tends to be maintained at its normal concentration by the influx from and depletion of water reserves in the skin and muscles, so that if the loss is not too prolonged serious functional effects are avoided. If, on the other hand, water loss is rapid, the blood is not maintained at its normal concentration and severe functional disturbances occur.

Thus, in severe rapid dehydration, with the reduction in blood volume, there occurs an increase in the red blood count, the Hb percentage, the serum proteins and the N.P.N. and urea, sugar, etc., the whole blood chlorides usually being decreased. In the more chronic type of dehydration, with the water loss persisting over several days, there is a gradual change in the picture. A second factor, namely, the toxic destruction of protein results in a drop in the red blood count and the Hb percentage, a fall in the serum proteins to quite low levels and a further increase in the N.P.N. and blood urea. The whole blood chlorides may remain normal or become slightly elevated.

These changes in the blood picture result in certain functional disturbances in other organs, for example, in the kidney and the liver. The presence of albumin and casts in the urine point to kidney damage, and an oliguria becomes marked, not only because of the lack of available water for excretion, but also because of the difficulty in the production of urine against a blood of high osmotic pressure. Liver damage is shown by the presence of urobilin in the urine, the polygonal cells of the liver being unable to utilize the circulating urobilinogen.

Dehydration also results in the production of fever. 87% of the heat lost to the body occurs by way of the skin. The heat is carried to the skin by water and some of it is lost through the skin with water. If the water reserves of the body are depleted, heat loss is prevented and fever occurs. The inanition fever of children is a common example of a mild dehydration, relieved by the administration of water alone.

Alterations in acid base balance constitute a third serious factor in dehydration. Acidosis or alkalosis may be produced, depending upon the type of ion lost with the water. This in turn depends largely upon the route of the water loss.

For example, in the group of vomiting cases, gastric juice and gastric mucus are lost to the body. These secretions contain a large proportion of chloride ion and their loss constitutes a greater drain on the blood chloride than upon the blood base. This loss is compensated for mainly by an increase in the HCO_3, but partly by an increase in the phosphate, sulphate and organic acids. This results in an alkalosis, the severity of which is mitigated to some extent by the accompanying loss of base.

In the group of diarrhoeas, the picture is somewhat different. Of the intestinal secretions, the pancreatic juice contains fixed base, mainly sodium, in large excess over chloride ion. The bile and jejunal secretions contain base and chloride in approximately the same proportion as plasma. The loss of these secretions, therefore, result in the loss of slightly more base than chloride ion. In addition, in diarrhoea, the sodium and potassium usually excreted in the urine or stored in the body is lost in the stools as well as increased amounts of calcium and magnesium. The ratio of base to acid in the stools in this condition is about 1.2 to 1. There is, therefore, a pronounced drain on the alkali stores of the body and this results in acidosis.

In diabetes mellitus acetone bodies are produced. These substances being relatively strong acids, unite with base and are excreted in the urine. Base is constantly being removed from the blood and acidosis results.

In the treatment of dehydration, it is important that the cause be dealt with, although this may have to wait until the dehydration itself has been somewhat relieved. In the acute stage, before destruction of the red blood cells or serum proteins has occurred, water alone by mouth is usually sufficient. In the later stages, it is necessary to administer NaCl and water intravenously. It is essential that sufficient water be given to allow for the re-establishment of kidney function, otherwise hyperchloraemia may ocrur. The re-establishment of kidney function aids in the correction of the disturbed acid base balance by allowing for the elimination of excess acid or base in the urine. The addition of glucose to the NaCl and water intravenously is of value. It tends to decrease protein breakdown, helps to get rid of ketone bodies and stimulates kidney activity.

The two clinical dehydrations, miner's cramp and diabetes insipidus, are of interest, in that under certain conditions, a further derangement of water balance, namely, water intoxication, is developed.

Miner's cramp derives its name from the fact that it occurs frequently in miners doing hard physical work in a superheated atmosphere. Perspiration is profuse. They lose water and NaCl through the skin as sweat and so become dehydrated. If now large quantities of water are administered, muscle cramps develop. This does not occur if saline solution is used.

In diabetes insipidus, there is polyphagia and polyuria. Dehydration occurs if the fluid intake is restricted. The administration of pituitary extract decreases the desire for water and the urine output returns to normal. If, however, the accustomed large quantities of water continue to be taken, symptoms similar to miner's cramp, although in a more exaggerated form, develop.

Rowntree, Harding and others were able to produce the following chain of symptoms in animals by the administration of 50 cc. water every half hour for from five to nine hours—salivation, tremor, weakness, muscle cramps, convulsions and death. These symptoms were not produced by the administration of normal saline solution in similar

amounts. The blood picture is that of an hydraemia. It would appear that in these experiments, as in miner's cramp and in the treated diabetes insipidus, the underlying disturbance is that of excess water in the body, unaccompanied by adequate amounts of NaCl. The administration of hypertonic saline solution, usually, 10%, relieves the condition, even in the convulsive stage.

The last disturbance in water balance to be discussed is oedema. Oedema is a condition in which fluid accumulates to an abnormal degree in the tissue spaces, lymph vessels and serous cavities of the body, together with a varying degree of increased fluid in the cells themselves. There are two main theories of oedema formation.

The colloidal theory states that there is a change in the colloidal state of the protoplasm, so that cells may imbibe or lose water.

The physico-chemical theory postulates that oedema occurs because of an upset balance between such factors as filtration, osmosis and diffusion, which normally regulate the flow across cell membranes. In this connection, Na appears to be of the utmost importance. Oedema can be produced by an intake of 35-40 gms. of NaCl daily. It is not produced by any of the other salts of chlorine. In fact, they all act as powerful diuretics. On the other hand, sodium bicarbonate administered in doses of 15 grams daily produces oedema, as does a number of other sodium salts in similar dosage. Sodium is antagonistic to Ca in this respect and when the normal ratio in the plasma is disturbed, oedema occurs.

Another factor in the production of oedema is serum protein deficit. It is known that when the plasma albumin falls below 2.5% and the total plasma protein below 5.5%, oedema is apt to occur. That this may readily occur is evident when it is realized that in nephritis as much as 5 to 20 grams of protein may be excreted daily. Thus in ten days there may be 100 gms. albumin lost and the total blood albumin of a 70 kilo man is only about 140 grams. Since it takes eight to ten days to replace half of the plasma proteins after plasmaphoresis, it is obvious that it might be almost impossible for the organism to replace the albumen lost to the body and so oedema is inevitable.

In cardiac oedema, there is increased hydrostatic pressure in the capillary bed. This may produce actual cellular or capillary damage as well as the injury due to deficient oxidation of the capillary and tissue cells. The oedema fluid is of the same composition as the interstitial fluid.

Nephritic oedemas arise from different causes, depending on the precise kidney condition present. In acute nephritis, there is increased permeability of capillary cells due to the action of the bacterial toxin. In subchronic and chronic nephritis and in nephrosis, the oedema when present is usually due to plasma protein deficit, although in the end stages, it is due to the actual inability of the kidney to excrete water. Nutritional oedema or war dropsy is due also to plasma protein deficit.

Pulmonary oedema is said to be entirely a pressure effect, because of engorgement of the pulmonary vessels.

The oedema of inflammation and of allergy is due to increased permeability of the capillaries, the one caused by bacterial toxin mainly, and the other by a little understood mechanism allied to protein shock.

The treatment of oedema again depends on the type. Water restriction is common to all types. NaCl restriction is of value, in that it may prevent or decrease oedema, even if due to low protein levels in the blood. The use of such substances as ammonium chloride, calcium chloride, etc., produces a diuresis and so may decrease the oedema. Magnesium sulphate increases the loss of fluid by bowel. Diuretics, such as novasural, urea and digitalis, etc., may be used when indicated. Finally, when there is plasma protein deficit, high protein intake is of value,

provided other conditions do not prohibit its use.

In conclusion, it may be said that it is evident from this short review that derangements in water balance may be superimposed upon almost any pathological condition. It is important that the nature of these changes be recognized in order that suitable treatment may be instituted to prevent or relieve the condition.

What Is the Social Objective of the Young Physician?

N. B. Van Etten. J.A.M.A., Mar. 7, 1936.

During the month of March most medical students become discouraged at the tremendous number of facts which loom in the pathway to a successful completion of the academic year. One knows that a very large proportion of the detail of notes and clinical instruction will be forgotten. That which is of practical use will be recalled repeatedly until it cannot evade the memory whereas academic points of little practical value will most often be completely forgotten.

If such thoughts depress one, an excellent treatment would be the perusal of the subjects of this review. Dr. Van Etten discusses the qualifications of the graduating students applying for internship in an approved hospital of New York State. He presents some of the type questions of internship examinations and compares the answer received with the desired one. He deplores the fact that most students have a detailed knowledge of the facts of medicine but have very little appreciation of their relative importance. Especially does he regret the general tendency to treat the disease rather than the patient.

However, he does not criticize destructively so much as constructively, recognizing that education of students is a far more difficult procedure than the dictation of lecture.

For the student who would like to obtain the viewpoint of an examiner on the requirements of an excellent medical student, this two-page article should prove very profitable.

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ARTIFICIAL PNEUMOTHORAX AS A METHOD OF TREATMENT IN LOBAR PNEUMONIA

By G. W. CRAGG, M.D.
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Induced or artificial pneumothorax, although a recognized form of treatment in other forms of pulmonary disease, is a comparatively new form of armamenteria in the hands of physicians in combatting the dread ravages of pneumonia. The first mention of this form of therapy is made by Rood of the United States Army Medical Corps during the influenza epidemic of 1919. He treated some the his influenzal pneumonia cases by lung puncture, and he made the statement that many of these cases with severe pleural pain were relieved, especially if pneumothorax occurred. He also noted that many showed a critical fall in temperature at the same time, but there the matter dropped. In 1921 Friedmann, working on the assumption that splinting any inflamed structure was ideal treatment, induced artificial pneumothorax in six patients with remarkable success. Other physicians reported odd cases up to 1932. when Coghlan in London, reported six cases treated by pneumothorax with such remarkable results that interest was stirred and led Leopold and Liebermann in Philadelphia to experiment on dogs. Thirty-six dogs were given pneumonia by injecting virulent pneumococci intra-tracheally, and eighteen were treated with artificial pneumothorax and eighteen kept as controls. Of the treated dogs fifteen recovered and of the controls only five recovered. This startling result started a wave of clinical investigation and in the past two years some one hundred and ninety-two cases have been reported on.

Various opinions have been expressed regarding the efficacy of pneumothorax as a treatment for lobar pneumonia. Nearly all agree that it is a rational form of therapy and much benefit results from its use. Approximately fifty per cent. of the cases treated have had what appeared to be an artificial crisis, and only on very rare occasions has pneumothorax been at all detrimental to the pneumonia patient, and this in one of the cases where inexperience may have been a factor in the fatal outcome.

Up to the present time hardly enough cases have been reported to give an accurate estimate as to whether the mortality rate has been lowered. In 1935 Leopold and Liebermann collected one-hundred and ninety-seven cases treated by this method. Of these fifty-nine cases died, giving a mortality of 29.4 per cent. This figure is reported mainly from centres where the mortality rate ordinarily runs as high as 50 per cent. In the same year Behrend and Cowper, in a controlled series of cases, found that the mortality in the control group was fifty-one per cent., whereas in the treated group the mortality was thirty-five per cent.

Factors Influenced by Pneumothorax.

Pneumothorax does three things which are of greatest value to the patient struggling for life against the pneumococcus. First, it relieves pleural pain. Pleural pain in pneumonia is one of the greatest factors in wearing down a patient's resistance. It is the cause of the rapid, shallow, grunting respirations which all are so familiar with. It is the factor which prevents rest, so needful to the pneumonia patient. Whether one accepts the theory that pain is caused by the rubbing together of the two inflamed

pleurae or by the stretching of an inflamed pleura, the introduction of air relieves the pain, either by separating the pleurae or reducing the tension of the inflamed tissue. It is a great satisfaction to see a patient, labouring for breath before pneumothorax, begin to breath deeply and freely, and to note the look of relief come over the patient's face and to come back half an hour later and find him sleeping peacefully without sedative.

The second thing which pneumothorax does is to relieve cyanosis. Not infrequently we have seen patients deeply cyanosed become pink and rosy after a treatment. This is probably due to the freer ventilation allowed by the relief of the restriction to respiration, occasioned by pain.

The third greatest factor is the reduction of toxaemia. In about fifty per cent. of cases, within one to four hours after the initial pneumothorax, the temperature, pulse and respirations begin to fall, blood pressure rises and leucocyte count falls, and frequently a profuse perspiration takes place and all the appearances of a natural crisis are seen. In the majority of cases a second pneumothorax in eighteen to thirty-six hours is necessary and from this time on a normal convalescence ensues. Why toxaemia is reduced is not definitely known, but it is believed to be due to the diseased lung collapsing down on itself and closing off lymphatic drainage. Although not proven, certain experiments carried out by Leopold and Liebermann recently have strongly suggested this to be the case. In our experience also it has been found that not only is general toxaemia reduced but positive blood cultures become negative.

Selection of Cases.

From experience, it has been found that the earlier a case is treated the better will be the result. The optimal time seems to be within the first seventy-two hours. This is the time in which the lung is still a semi-fluid mass and will collapse to the greatest extent. After this time the lung becomes more solid and less collapse can be achieved.

Unilateral cases have been chosen exclusively up to the present, but we have treated bilateral cases with bilateral pneumothorax with utmost satisfaction.

In all cases before using this type of therapy, a careful history must be taken, careful and thorough examination made, and if at all possible, examination should be supplemented by an X-ray of the chest. Blood counts, blood cultures and typing of the organism from the sputum should be begun.

Wherever pain is present and the patient is in distress a pneumothorax, no matter to what stage the disease may have progressed, will be found to be of material benefit to the patient.

Method.

Having decided upon pneumothorax therapy, the patient should be prepared as carefully as for any surgical operation. The operator should also take the utmost aseptic precautions. Greater skill is required in inducing a pneumotmorax in pneumonia than in tuberculosis. The pleura in pneumonia being exceedingly friable, and dangers of tearing the visceral pleura and puncturing the lung are greatly increased, with the added danger of a pyopneumothorax resulting.

We have found that two injections of air are all that are usually required. These are given eighteen to thirty-six hours apart and the total amount usually does not exceed seven hundred cubic centimetres of air. We have found that maximum benefit with minimal possibility of complications, is achieved if the intrapleural pressure is not raised above atmospheric. Other workers have tried using large quantities of air, striving to attain complete collopse, but their results, while good, have not been quite as successful as where smaller quantities were used.

Findings.

We have found that in nearly all cases pain was promptly relieved. In one or two cases pain persisted, but on radiological examination it was discovered that pleural adhesions were present which prevented the separation of the two pleural surfaces. Relief from cyanosis was usually concurrent with the relief from pain. In approximately fifty per cent. of cases a prompt general improvement occurred with a critical fall in temperature and in nearly all cases the patients made the statement that they felt better and their general appearance supported their assertion.

We have found that the mortality rate in our series of cases was about fourteen per cent. as compared with thirty-three per cent. in all cases admitted with pneumonia, and that whereas in cases with bacteraemia the mortality is seventy to eighty per cent., our series has shown almost exactly the reverse, with seventy to eighty per cent. recoveries.

Complications.

Certain complications will, and do arise. The most common is that of super-added spontaneous pneumothorax. This is probably due to tearing adhesions or puncturing the lung. It, in itself, is of no consequence and causes no distress to the patient, but may lead to the more serious complication of pyopneumothorax, which requires surgical drainage. We have found that the incidence of empyema has been increased by approximately twenty-five per cent., but this may be due in part to the recovery of patients who had a bacteraemia.

Summary.

On the whole, artifical pneumathorax in the hands of a trained individual,—and only a skilled practitioner should attempt this form of treatment,—has been of decided advantage in treating lobar pneumonia by adding to the comfort of the patient and by reducing mortality rate. Anyone who is reasonably skillful can learn to do this type of procedure quickly but here I would add the warning—"pneumonia patients are not the ones to practise on."

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DIVERTICULOSIS AND DIVERTICULITIS

DONALD G. H. MacDONALD, B.A., '37

Diverticulitis is a condition which has not yet received the attention it deserves. To quote, "complete recognition has not yet been accorded this malady, for neither has it been given that place in the current text-books of medicine and surgery that its frequency and importance demand, nor has it fully entered into the clinical consciousness of the general medical practitioner." In this article, discussion is confined to the formation of diverticula of the large bowel, to secondary changes in them, and resulting complications. A discussion of diverticulitis in general is too great a study for one paper.

Historical.

The condition of diverticulitis of the colon was first reported in 1849 by Cruveilhier and a few years later, 1853, Virchow described a condition of peridiverticulitis. In 1858, Sidney Jones recorded the finding of sigmoid diverticulitis with bladder fistulae. However, these findings were post-mortem findings, and it was not until 1898 that Graser directed attention to diverticulitis as a cause of sigmoid symptoms. In 1907, Mayo published results of surgery on acute cases of diverticulitis. The last milestone to be mentioned is the diagnosis, by Abbe, in 1914, by the use of X-ray, of the condition prior to operation.

Definition.

Diverticula may be classed as true or false, acquired or congenital, mechanical or inflammatory. The diverticula considered in this account are false and acquired and the condition is known as diverticulosis. Diverticulosis may be defined as a relatively frequent condition of unknown origin consisting of a herniation of the mucosa and submucosa of the large bowel through the muscle coat and rarely manifest by symptoms. These diverticula are usually the size of a large pea and vary in number reaching a frequency of 400.

Incidence.

Of 26,699 X-ray examination of the colon at the Mayo clinic for general diagnostic purposes, 1,574 cases of diverticula were found, i.e., the incidence was 5.89%. Of these 1,574 cases of diverticulosis, only 16 were under the age of 40, and 653 had diverticulitis. In this series, 64% were males and 36% females. In Edwards' series, the incidence of diverticulosis and diverticulitis in cases with a lesion requiring X-ray examination of the bowel was 10.8%, the average age of the patients being investigated was 60, while the duration of symptoms was, on the average, 7½ years. Hence the onset of diverticulosis is placed between the ages of 40-45, and although cases at 7 and 8 years of age are on record, it is considered a disease of middle life. In general, we may say that the incidence of diverticulosis amongst those over 35 years of age is approximately 5%, and of this 5%, 12-15% develop diverticulitis.

Location.

Diverticula occur elsewhere along the alimentary canal besides the colon, where they are most frequent, being next most common in the ileum, then oesophagus, then pharynx, then duodenum and, least of all, in the stomach. Local conditions of the colon favour the development of diverticulitis more than elsewhere. In Masson's series of 116 cases, they were located as follows: caecum, 4%; transverse colon, 3%; descending colon, 4%; sigmoid, 81%; rectum, 4%; not located 4%. Thus it is seen than in 90% of cases, the condition develops distal to the splenic flexure of the colon.

Etiology.

In considering the reasons for diverticula formation, there are many facts and theories to be mentioned. The incidence in middle life suggests that they are acquired, their occurrence in local segments suggests local disease rather than mechanical cause. Obesity may be a factor, as the patients are usually overweight. Constipation may also be a factor, yet 65% of the cases are males, while constipation occurs twice as often in women. Hereditary tendencies have also been noticed.

At present, there appears to be two chief schools of thought, of which Spriggs and Marxer represent one and Edwards the other. Spriggs and Marxer speak of a pre-diverticular state, a stage of formed diverticula or diverticulosis and a stage of inflamed diverticula or diverticulitis. The pre-diverticular state was first recognized in 1920 by Marxer. Radiographically, there is "a ragged outline of the wall of the bowel, which does not dilate, even in the most favourable position and normal segmentation is lost." This state they believe to be due to inflammation, which slowly creeps along the bowel wall. At first, the bowel shows a rigid outline with small convexites, followed by irritation of the bowel, giving an irregular concertina outline. Later, the bowel becomes flabby and diverticulous.

Edwards, however, states that the pre-diverticular state is one of irregular atrophy and relaxation of the circular muscle, alternating with areas of contraction and hypertrophy. He also emphasizes the facts that the points on the circumference of the intestine through which the diverticula emerge are governed by two anatomical factors, the longitudinal muscle and the mode of entry of the blood vessels, of which there are two sets. The site of election is to the mesenteric side of the lateral taenia, in which position they are hidden in an appendix epiplocicae often. Starting as a hernial diverticulum, a wedge-shaped mass of mucous membrane penetrates the circular muscle at the point of entry of a blood vessel. The internal pressure forces the mucous membrane along the connective tissue sheath of a blood vessel and simultaneously the circular muscle contracts or hypertrophies, narrowing the bowel lumen. If there is a vessel, or area of fat infiltration, at an area of atrophy, herniation occurs. The blood vessel has been likened to the spermatic cord in inguinal hernia. The longitudinal muscle exaggerates the normal sacculations and the migration of the mucous membrane narrows the mouth of the diverticulum.

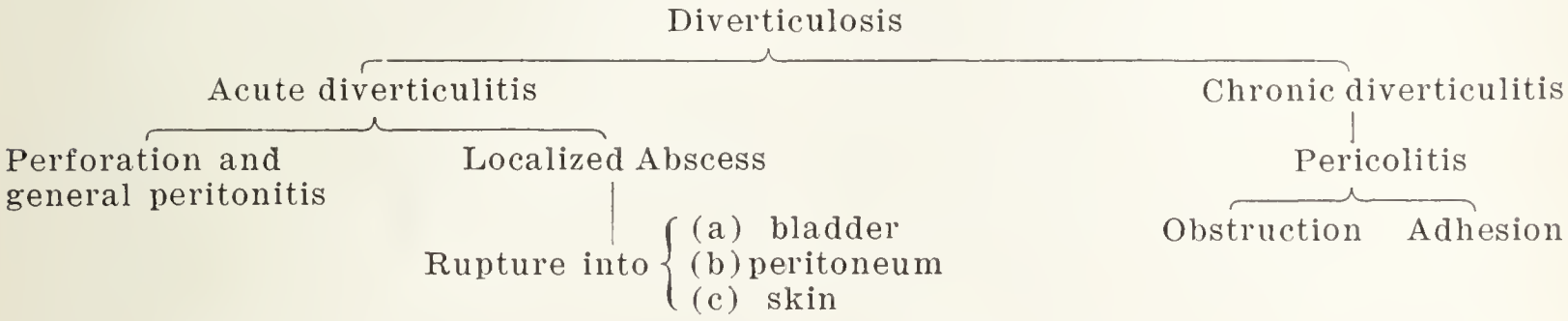
d'Abreu also agrees that the cause is spasm and hyperactivity of the circular muscle of the bowel and believes that this is due to excessive para-sympathetic activity. He mentions the development of the pre-diverticular state with spastic irregularity in several of his patients, in whom a presacral and lumbar colonic neurectomy had been performed. He has had considerable success treating cases diagnosed as pre-diverticular with belladonna and atropine. His cases are usually fat, middle-aged men of sane outlook, who have noticed an altered bowel habit and in whom there is no neoplastic, ulcerative, or fully developed diverticulous disease, but who have abdominal pain, usually on the left side, blood or mucus in the stools and occasionally irritative diarrhoea and constipation.

Seymour Barling first observed the prediverticular condition, operating under local anaesthetic, which does not completely reduce bowel tone. He found that the colon showed red areas that go into spasm, suddenly contracting to the size of the index finger, becoming intensely rigid, with pearl-like buds extruding in series between the taenia. As the spasm passes off, these disappear. The combined effect of the presence of solid contents and the high degree of excitability of the sigmoid explain why it is to the most common situation for the development of diverticula.

To summarize the etiology, it may be said that inflammation is always secondary to the formation of diverticula and is then due to foreign bodies or faecal matter getting into the formed diverticula and that the earliest stage in the development of diverticulitis is the formation of pulsion diverticula in the colon wall, due to weakness of the musculature at areas of entrance of blood vessels which may be altered by passive congestive conditions or cardio-vascular disease.

past the muscle coat. At the latter stage, when past the muscle, they form the typical globular outline with narrow necks at the original point where they pierced the mucous membrane. These diverticula appear to increase in number, despite any form of treatment.

Once the anatomy of diverticulum has been appreciated, together with the fact that there is a tendency to fecal retention, the secondary changes can almost be anticipated on theoretical grounds.



X-ray.

The dilated part of the diverticulum is extraluminal, hence if filled with barium, there is an opaque, flask-shaped, rounded shadow projecting from the bowel. This, together with the fact that these pockets retain the barium long after the lumen of the bowel is empty, identifies this condition. One important point is that a thorough emptying of the large bowel should take place before giving the barium enema. In this way, if central translucent areas are seen surrounded by opaque lines of barium, the presence of concretions not moved by the douch are indicated. It is to be remembered that the formation of these concretions distinguish diverticula of the large bowel from diverticula elsewhere and lead to diverticulitis.

The development of diverticula may also be studied by X-ray. The very first sign is the serrated outline to the colon which, to review, Spriggs and Marxer state to be due to inflammation, but which others state to be due to numerous diverticular buds in the colonic wall. These tend to broaden on getting

The sequence of events may thus be summarized by the foregoing diagram. Once a diverticulum is formed, it tends to undergo progressive enlargement. The chief reasons no great size is attained is that secondary changes supervene and that diverticula develop so late in life, there is time neither for the attainment of considerable size nor the development of any serious degree of secondary inflammation. Since a diverticulum is sac-shaped with a narrow neck, faecal contents tend to be retained and form concretions of stony hardness. The main mechanical result of this is perforation. If the tip of this concretion projects into the main faecal mass, sudden trauma or peristalsis may lead to pistol shot perforation without preceding marked inflammation. The usual secondary change is an inflammatory process of varying type and intensity. This is due to the mechanical irritation of the faecal mass, combined with the presence of micro-organisms. Drainage of the sac is poor, due to the small neck and toxic oedema of the lipped orifice. In this way, an acute or gangrenous inflammation is determined. In addition to the inflammation

of the sac wall, there is very liable to occur a low-grade, chronic, hyperplastic inflammation around the diverticulum. This process may become very marked, and may surround the diverticulum. A section of gut may be surrounded by a constricting band of fibrous tissue leading to tumour formation by its hyperplasia and stenosis of the gut by its contraction. To this, the term peridiverticulitis has been applied. It is due largely to the low inflammatory reaction induced by the leaking into the tissues of bacterial toxins through the damaged sac walls; possibly in addition to the passage of a certain number of organisms of low virulence.

Keeping in mind that diverticulitis is a primary pathological entity, with various manifestations, the following secondary pathological results may be described.

(a) Mechanical.

1. *Formation of Faecal Concretions* —The reasons for formation of concretions has been given. Such a rough-surfaced concretion in a thin-walled sac will set up a mechanical irritation, aided by the mobility of the sigmoid loop, favouring inflammation. Such a concretion will aid forces in the bowel to cause perforation.

2. *Torsion of a Diverticulum*—If the diverticulum forms a pedunculated sac, or is in a large appendix epiploica, elongation and twisting of the neck is favoured, leading to constriction of the neck or the formation of a loose body in the peritoneum.

3. *Lodgment of foreign bodies.*

(b) Inflammatory.

1. *Inflammation of the Wall of the Diverticulum (diverticulitis)*—In the acute and gangrenous types, all the phenomena of acute appendicitis are present in the left lower quadrant. Chronic inflammation occurs, with hyperplastic diverticulitis and is a predisposing cause of sudden rupture.

2. *Passage of Organisms without Perforation*—While organisms cannot pass a normal intestinal wall, in the case of the diverticulum, the wall is damaged and inflamed and greatly thinned. Thus an inflamed diverticulum may be the cause of a general peritonitis of unknown origin.

3. *Peridiverticulitis* — This is a chronic proliferative inflammation, tending to thickening and stenosis of the bowel. An annular band is formed, which leads, in the first place, to tumour formation and later to actual stenosis of the bowel. Rupture of diverticula into such a mass lead merely to the formation of pockets of pus, which are shut off from the general peritoneal cavity. It was this type of diverticulitis that was often mistaken and removed for carcinoma. Since the hyperplastic thickening may be extreme, up to two inches, and since the diverticula are carried from the lumen of the bowel, with narrowing of their original lumina, the original condition may be observed.

4. *Perforation of the Diverticulum* —This may give rise to a general peritonitis, localized peritonitis, localized abscess, or fistula. Due to the chronic nature of the diverticulitis and the peridiverticulitis, the sac about to perforate is frequently shut off by adhesions and a local abscess merely forms. These small abscesses make operation troublesome in this condition.

Fistula formation is common, especially if the diverticulum is already adherent to a neighbouring viscus. Sigmoido-vesical, recto-vesical, sigmoido-uterine, anal and external fistula have been noted, of which bladder fistulae are the most common. More fistulae are due to diverticulitis than carcinoma.

5. *Formation of Adhesions* — This tendency is obvious and produces startling results—acute intestinal obstruction, bladder symptoms or pelvic syndromes.

6. *Local Chronic Peritonitis* —This is a pericolitis sinistra, and is probably due to the leaking of toxins from the damaged sac walls, which leads to the formation of adhesions. Chronic peri-

tonitis of the sigmoid is very common and the explanation may be minute, multiple, microscopic diverticula.

7. *Chronic Mesenteritis of the Sigmoid Loop*—Contraction of the mesentery will lead to intestinal obstruction and symptoms of various kinds.

8. *Development of Carcinoma* — Opinion on this question is divided. It may be pointed out that the incidence of carcinoma of the colon is much higher than that of diverticulitis. Rankin and Brown, in 227 cases of diverticulitis, found four with carcinoma and in another series of 679 operations for carcinoma of the colon, found diverticulitis in only four instances. Hence we may with reasonable assurance dismiss the possibility that diverticulitis bears a causative relationship to malignant disease of the colon.

Symptoms.

A few words may be said of symptoms. With the onset of inflammation, diverticulosis loses its asymptomatic character and produces indications of its presence. There are recurrent attacks of abdominal discomfort, less often pain, not related to food, located in the lower abdomen, usually in the left iliac fossa. General flatulence and a feeling of distension are usually mentioned. Constipation as a rule, with occasional bowel irregularity, occasional diarrhoea and incomplete evacuation are present. This long-standing history of constipation, with occasional diarrhoea and left-sided colicy pain, is common. Tenderness is elicited by palpation and usually accompanied by more or less definite muscular rigidity. A tender, sausage-shaped tumour, varying in size and consistency, can be found in the left iliac fossa or bi-manually through the rectum and vagina. There is often leucocytosis and mild pyrexia.

Clinically, there appear to be three main types of diverteuilitis — the inflammatory, the obstructive and the genito-urinary types.

1. The inflammatory type has been called left-sided appendicitis. There is a tumour in the left iliac fossa and pyrexia. The manifestations of this type are protean. Often the first indication is a generalized peritonitis as a result of pistol-shot perforation at a time when adhesions were not formed. Obstruction may be produced, due to occlusion of the lumen by inflamed, oedematous mucosa folds. Usually there is merely the elongated, tender swelling in the left iliac fossa and pyrexia, the tumour varying in size from that of a sausage to that of a large phlegmonous mass. If treatment is successful, the tumour diminishes and the symptoms subside, clearing up in ten days.

2. The obstructive type is often mistaken for carcinoma. There is increasing constipation, tending to recurrent partial or incomplete obstruction, pain, tenderness in the left iliac fossa, pyrexia and tumour. As soon as possible, a colostomy should be performed and an estimate of the condition obtained.

3. The genito-urinary type is uncommon, constituting 7% of cases. Here a vesico-colic fistula develops and the ensuing cystitis is serious. For this, after colostomy, C. H. Mayo separates the sigmoid from the intestine and bladder, sutures the fistulous openings, makes an opening into the omentum and brings the sutured portion of the sigmoid to the peritoneal surface of the abdominal incision and attaches it there by sutures. The omentum is thus thrown between the defects of the colon, bladder and adherent intestines, and if a leak occurs, there is a safe exit.

Treatment.

The treatment of diverticulosis and mild diverticulitis is medical, using low residue diets, avoidance of saline purgatives, which aggravate the condition, exhibition of liquid paraffin and low pressure saline bowel washouts. If treatment is successful, diverticulitis subsides or if of diverticulosis, diverticulitis does not develop. Definite indications are required for operative inter-

ference. In acute cases that do not subside on medical treatment, drainage of the large bowel by colostomy or caecostomy is indicated; in cases of perforation, closure of the perforation and bowel drainage should be done. In cases of abscess formation, the abscess should be drained extraperitoneally before fistula formation. In chronic inflammatory cases with fistula or obstruction, the adhesions should be freed and the area wrapped in omentum, a colostomy or caecostomy performed and two or three months later, excision of the diverticulous area by means of a Paul-Mikulicz type of operation. A primary incision and suture can be performed only in unusual cases, where the disease is well localized and the bowel itself free on either side.

In this article an effort has been made to briefly follow the development of diverticulitis from the earliest stage, with formation of pulsion diverticula of the colon wall due to spasm and weakness of the musculature, through the stage of secondary inflammation, with its protean manifestations, to the stage of complications, requiring active treatment. It has been emphasized that 5-10% of those over the age of 40 have diverticulosis and 12-15% diverticulitis. It has been pointed out that symptoms depend on pathology and that the X-ray is useful in diagnosis. It has been indicated that the treatment of diverticulosis and mild diverticulitis is medical and of severe diverticulitis is surgical. Plastic operation must be preceded by colostomy or caecostomy.

ABSTRACTS FROM CURRENT LITERATURE

Pulmonary Rest by Posture.

P. H. Pierson & R. R. Newell: Am. Review of Tuberculosis: 1936: **33**: 1.

For years it has been thought that the movement of a lung would be a minimum when the patient was lying on the same side. From a superficial consideration this would seem to be responsible, for the ribs are unable to move as much on the under side and the mediastinum should fall, decreasing the volume of the under side of the thorax and compressing the lung.

However, this is not the case unless the diaphragm is paralysed on the under side, for Pierson & Newell have studied the problem experimentally in dogs, normal and tuberculous humans. In human subjects serial X-rays were taken with the individual lying on first one, then the other side. It was observed that on the down side, although the ribs moved very little, the excursion of the diaphragn was much greater. The converse is true for the upper side, so that it appeared likely that the tidal air was not decreased in the lower lung.

By tying a cannula into each bronchus in dogs, actual measurements of tidal aid showed that when the shoulders were raised (as by a pillow in the human) the tidal air in the lower lung appeared to be somewhat greater than in the upper.

Two radiographs of a patient with a large calcified nodule in one lung are shown, in which the patient is lying on first one side, then the other. This shows very clearly that the upper lobe of the lung moves down nearly as much as the diaphragn, which has been shown to move much more on the under than the upper side. Therefore, it is the lung of the upper side that is rested the most.

An exception to this rule is the case where phrenectomy has been done. In this case, if the diseased lung is on the upper side, no movement is possible, for the under side of the chest cannot expand and the diaphragm is paralysed.

J.P.F.

The Nature of the Peripheral Resistance in Arterial Hypertension.

Prinzmetal & Wilson: J. Clinical Investigation: 1936; **15**: 63.

The arm plethysmograph was used to measure the blood flow through the arm under the following conditions:

(1) Resting. Since the kidneys, adrenals, and pancreas show the most severe vascular lesions in hypertension, it is conceivable that the blood flow will be limited through the splanchnic area and increased through the periphery. However, investigation showed that the resting blood flow through the arm of hypertensive individuals is no greater than in normal ones.

(2) At temperature of .42 deg. C. and in reactive hyperaemia. In order to see if dilatation of arterioles occurs in hypertension to the same degree as in normal vessels, the arm is placed in a bath at 24 deg. C. and blood flow measured. The temperature is now raised to about 42 deg. C. and blood flow measured. Also, blood flow is measured before and after reactive hyperaemia. There was no abnormal response in hypertension.

(3) After vasodilatation by the vasodilator nerves. After stimulation of the vasodilator nerves by heat or novocaine injection into the dorsal sympathetic ganglia, the blood flow was measured. Normal responses were obtained both in benign and malignant hypertension.

Therefore, the authors conclude that the cause of hypertension must be an intrinsic response of the vessel wall to some stimulus.

J.P.F.

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